Supreme Court, U.S.
FILED
DEC 9 1985
JOSEPH F. SPANIOL, JR.
CLERK

85-981

No. ——

IN THE

Supreme Court of the United States

OCTOBER TERM, 1985

CONTACT LENS MANUFACTURERS ASSOCIATION,
Petitioner,

v.

FOOD AND DRUG ADMINISTRATION OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,
Respondent.

On Petition for Writ of Certiorari to the United States Court of Appeals for the District of Columbia Circuit

APPENDIX TO PETITION FOR WRIT OF CERTIORARI

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APPENDIX A

UNITED STATES COURT OF APPEALS FOR THE DISTRICT OF COLUMBIA CIRCUIT

SEPTEMBER TERM, 1984

No. 84-1025

CONTACT LENS MANUFACTURERS ASSOCIATION,
Petitioner

v.

FOOD & DRUG ADMINISTRATION OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,
Respondent

Petition for Review of an Order of the Food & Drug Administration

Before: ROBINSON, Chief Judge, WALD and GINSBURG, Circuit Judges.

[Filed July 9, 1985. George A. Fisher, Clerk]

JUDGMENT

This cause came on to be heard on the petition for review of an order of the Food & Drug Administration, and was argued by counsel. On consideration thereof, it is

ORDERED and ADJUDGED, by this Court, that the petition for review herein is dismissed and the challenged decision is hereby affirmed, in accordance with the Opinion for the Court filed herein this date.

Per Curiam
For The Court
/s/ GEORGE A. FISHER
George A. Fisher
Clerk

Date: July 9, 1985

Opinion for the Court filed by Circuit Judge Ginsburg.

APPENDIX B

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

No. 84-1025

CONTACT LENS MANUFACTURERS ASSOCIATION, PETITIONER

v.

FOOD & DRUG ADMINISTRATION OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, RESPONDENT

Petition for Review of an Order of the Food & Drug Administration

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Argued February 26, 1985

Decided July 9, 1985

Daniel J. Manelli, with whom *Edward A. Scallet* was on the brief, for petitioner.

Beverly Sherman Nash, Attorney, Department of Justice, *Richard K. Willard*, Acting Assistant Attorney General, *J. Patrick Glynn*, *Margaret A. Cotter*, *Mark H. Gallant*, Attorneys, Department of Justice and *Michael M. Landa*, Attorney, Food and Drug Administration.

Before: ROBINSON, *Chief Judge*, WALD and GINSBURG, *Circuit Judges*.

Opinion for the Court filed by *Circuit Judge* GINSBURG.

GINSBURG, *Circuit Judge*: In 1938, Congress armed the Food and Drug Administration (FDA) with authority to prevent the marketing of hazardous drugs. By the mid-1970's, however, it had become apparent that the legislature's delineation of the FDA's domain was too narrow to enable the agency to protect the public from some of the most dangerous health care products. Mindful of recent misfortunes involving faulty pacemakers and the Dalkon Shield, Congress enacted the Medical Device Amendments of 1976 (Amendments or statute), Pub. L. No. 94-295, 90 Stat. 539 (codified at 21 U.S.C. §§ 360c-360k (1982)), thereby extending the FDA's premarket surveillance field beyond drugs to medical devices. This case, one of first impression, involves the FDA's administration of the Amendments.

Congress' new prescription for the FDA divided the world of medical devices into three classes, according to the degree of regulation thought necessary to provide reasonable assurance of each device's "safety and effectiveness." Class I encompassed devices whose safety and effectiveness could be reasonably assured by "general controls" set out in various sections of the Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301-392 (1982). Class II covered devices that posed somewhat greater risks; devices placed in this category would be subject to "performance standards" in addition to the residual general controls. Class III was to obtain devices (1) whose safety and effectiveness could not be reasonably assured by any combination of general controls and performance standards, and (2) whose purported purpose was to aid in supporting or sustaining human life or preventing its impairment, or whose availability presented "a potential unreasonable risk of illness or injury." No device consigned to class III could be sold to the general public until, through a costly and time-consuming process, it had gained the FDA's "premarket approval." *See* § 360c (a) (1) *id.*

Congress itself was not positioned to determine the appropriate classification of every medical device then in existence or yet to be invented; nor could it describe the statutory categories with sufficient precision to ensure that each device would simply fall into the proper class of its own accord. The legislators therefore charged the FDA with the task of implementing the Amendments, and thus of essaying judgments appropriate to ensure safe and effective medical devices without stifling innovative technology. *See* H.R. REP. No. 853, 94th Cong., 2d Sess. 12-13 (1976) [hereinafter cited as HOUSE REPORT].

Congress drew several initial bright lines, however, that significantly affected the classification process. "[D]evices of a type introduced or delivered for introduction into interstate commerce for commercial distribution" before the date of the Amendments' enactment were to remain entirely outside the classification scheme until the FDA decided where to place them. *See* 21 U.S.C. § 360c(c)(3); General Provisions and Classification of 119 Devices, 47 Fed. Reg. 3694, 3694 (1982) [hereinafter cited as Mass Classification Proposal]. Devices introduced after the date of enactment, by contrast, would rank in class III unless shown to belong to a non-class-III family of devices and to be "substantially equivalent" to a particular, already-marketed device within that family. *See* 21 U.S.C. § 360c(f)(1)(A); 21 C.F.R. § 860.134 (1984). Moreover, under provisions labeled "transitional," class III ranking automatically attached to "[a]ny device intended for human use . . . which the [FDA] in a notice published in the Federal Register before the enactment date has declared to be a new drug." 21 U.S.C. § 360j(*l*)(1)(E). The FDA could later reclassify any device that, for whatever reason, had been "overclassified," but this remedy required a proffer of "new information," *id.* § 360c(e)—or, as the FDA formulated the standard, "valid scientific evidence" of safety and effectiveness. 21 C.F.R. §§ 860.7, .123(a)(6).

The instant petition concerns the first attempt ever to reclassify a medical device committed to class III by the Amendments' "transitional provisions." Contact Lens Manufacturers Association (CLMA) challenges the FDA's withdrawal of the agency's own proposal to transfer certain rigid gas permeable (RGP) contact lenses from class III to class I. 48 Fed. Reg. 56,778 (1983). Claiming that RGP lenses (and hence, RGP lens manufacturers) have suffered disparate treatment in relation to other medical devices (indeed, other contact lenses), CLMA urges that "something has gone very wrong here." Brief of Petitioner at 2. We conclude, however, that CLMA's travails are attributable to the intricacies of the legislation Congress ordered, and to the broad administrative discretion Congress conferred upon the FDA. Because our review satisfies us that the FDA has permissibly exercised its considerable discretion in this case, we affirm the agency's action.

I.

Contact lenses consisting almost entirely of polymethylmethacrylate (PMMA)—"hard" lenses—have been marketed in the United States since the early 1950's. *See* Regulatory Policy and Proposed Rulemaking for Marketing Contact Lenses, 40 Fed. Reg. 44,844, 44,845 (1975) [hereinafter cited as New Drug Notice]. Because the public's pre-Amendments experience with PMMA lenses was broad and substantially injury-free, *see id.*, these lenses will remain outside the Amendments' classification scheme until the FDA formally decides where to place them. *See supra* p. 3. That decision has not yet been made; three years ago, however, the FDA proposed to regulate PMMA lenses as class II devices. *See* Mass Classification Proposal, 47 Fed. Reg. at 3736.

Hydroxyethylmethacrylate (HEMA) lenses—"soft" lenses—are a more recent development. The FDA first approved a HEMA lens in 1971. *See* 47 Fed. Reg. 53,411,

43,415 (1982). In September 1975, citing their relative novelty, the FDA announced that HEMA lenses—indeed all lenses "other than those consisting [almost wholly] of PMMA"—had been and would continue to be regarded as "new drugs":

> This decision to regulate such contact lenses under the new drug provisions of the Federal Food, Drug, and Cosmetic Act was based on a recognition that new plastic materials that had not been shown to be safe and effective were being introduced for use in the manufacture of contact lenses. The introduction of these new materials led to new lens design and use, new manufacturing methods, and new methods for lens care. The Food and Drug Administration is concerned that the use of these contact lenses may result in serious eye damage if the new material of which they are composed is unsafe for use in the eye, if the user cannot feasibly care for the lenses, or if the highly complex procedures for the manufacture of these lenses are not carefully controlled to assure a product of uniform quality.

New Drug Notice, 40 Fed. Reg. at 44,845. This announcement rendered HEMA lenses class III devices under the Amendments' "transitional provisions." *See supra* p. 3; *cf. infra* note 3 (rejection of reclassification proposal).

The product at issue in this case is said to combine attractive features of both lens types described above. "RGP lenses" (like "PMMA lenses" or "HEMA lenses") is a generic term that indicates no single mix of polymers or manufacturing process; but all lenses properly called RGP share certain salient characteristics. The ideal RGP lens permits both the superior visual acuity attainable with a hard lens and the "direct transmission of oxygen to corneal tissue" that the hard lens regrettably prevents. *See* 47 Fed. Reg. 53,402, 53,406 (1982) [hereinafter cited as Reclassification Proposal]. Nearly a million peo-

ple in the United States wore RGP lenses in 1982. *Id.*[1] As of 1975, however, RGP lenses, like soft lenses, were comparatively new and untested; since enactment of the Amendments the FDA has regarded RGP lenses as "transitional" class III devices by reason of the same September 1975 *Federal Register* announcement that resulted in placement of HEMA lenses in the class III category. *See supra* p. 5; *infra* pp. 11-12.

Consequently, before a manufacturer can market a particular RGP lens to the public, the manufacturer must demonstrate the safety and effectiveness of that lens convincingly enough to gain the FDA's premarket approval. "[I]n effect," the manufacturer must obtain "a license to market the device." Brief for Respondent at 5 n.6. (If RGP lenses were class I devices, the manufacturer would be required to make the showing CLMA regards as less burdensome that the lens was "substantially equivalent" to another RGP lens already on the market. *See* 21 U.S.C. § 360c(f)(1)(A) (1982); *supra* p. 3. *But see infra* pp. 17-19.) The expense of obtaining a class III device license—"estimated at $750,000-$1,000,000 (over and above development costs)," Brief of Petitioner at 11, the bulk of which goes to clinical investigation—constitutes a significant barrier to entry. Not surprisingly, the first and largest of several manufacturers to surmount the premarket-approval hurdle, Syntex Ophthalmics, commands a dominant share of the market for RGP lenses. CLMA barely disguises its suggestion that Syntex is implicated in the FDA's decision to hold RGP lenses within the class III regime.

That decision did not follow a steady path. In March 1981 CLMA petitioned the FDA to reclassify RGP lenses from class III to class II. Pursuant to 21 U.S.C. § 360c(b)

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[1] Counsel for CLMA, demonstrating warm zeal for his client, informed the court in opening lines of oral argument that he and his co-counsel were themselves satisfied wearers of RGP lenses.

(1982), the FDA referred the petition to an expert advisory committee, the Ophthalmic Section of the Ophthalmic; Ear, Nose, and Throat; and Dental Devices Panel, which recommended the following month that the petition be granted on the condition that CLMA submit additional materials. In November 1981 the FDA announced that although CLMA's upgraded submissions continued to be inadequate, "CLMA's objectives are meritorious," and therefore the FDA intended to adopt the reclassification proposal as the agency's own. *See* 46 Fed. Reg. 57,648 (1981). The FDA promised to publish a formal proposal in a future issue of the *Federal Register*; meanwhile, the agency solicited comment on various economic issues that appeared unrelated to the lenses' safety and effectiveness. *See id.* at 57,648-49.

In November 1982, a year after the FDA's initial indication of interest, the reclassification proposal emerged.[2] "Based on a careful review of new, publicly available, valid scientific evidence," the proposal stated, "FDA has tentatively concluded that . . . certain [RGP lenses] should be reclassified into class I." Reclassification Proposal, 47 Fed. Reg. at 53,404. The proposal was limited to spherical lenses consisting of cellulose acetate butyrate (CAB) or polyacrylate-silicone. *Id.* But departing from CLMA's original request for class II designation, the proposal recommended reclassification down to class I. Although the FDA then "believe[d] that sufficient information exist[ed] to establish a [class II performance] standard," the agency also felt that safety and effectiveness could be adequately assured without such a standard. *Id.* at 53,405-06. The proposal extensively and

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[2] In the interim, FDA representatives had been questioned by members of a House subcommittee about the "rather unusual" delay. *FDA Oversight: Medical Devices: Hearing Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 97th Cong., 2d Sess. 3 (1982) (remarks of Rep. Whittaker); *see id.* at 29-34, 95-96, 104-06.

favorably discussed the clinical data cited by reclassification proponents. Nevertheless, the FDA invited comment on a range of issues including the following:

> 1. Do the data presented in this proposal constitute sufficient "valid scientific evidence" of safety and effectiveness to support reclassification of each [currently] marketed lens [and any lens that might be created] consisting of CAB or polyacrylate-silicone?
>
> ....
>
> 4. Does specifying the materials of which the lenses proposed for reclassification are principally composed adequately identify the lenses for the purpose of reclassification?

Id. at 53,410.

The uncertainty intimated by these questions soon became palpable. On December 10, 1982, the FDA extended the comment period thirty days, till January 26, 1983. 47 Fed. Reg. 55,497 (1982). On April 15, 1983, the comment period was reopened. 48 Fed. Reg. 16,293 (1983). A public hearing was held on May 26, 1983, followed by yet another fifteen-day comment period. *See* 48 Fed. Reg. 18,836 (1983). Finally, on December 23, 1983, CLMA's once high expectations for the RGP proposal ended: the FDA repudiated its "tentative conclusions" and withdrew its reclassification proposal altogether. 48 Fed. Reg. 56,778 (1983).[3]

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[3] CLMA's petition to reclassify HEMA lenses underwent a parallel odyssey and met an identical fate. Finding CLMA's January 1981 proposal deficient, the FDA itself took up the reclassification cause. 46 Fed. Reg. 57,648 (1981). A year later, the FDA formulated an official proposal to transfer HEMA lenses from class III to class I, and asked for comments. 47 Fed. Reg. 53,411 (1982). After enlarging the comment period, reopening it, holding a public hearing, and receiving more comments, the FDA killed the proposal on April 24, 1984. 49 Fed. Reg. 17,523 (1984).

The FDA attributed its changed view to "comments and oral and written testimony that required it to re-evaluate the evidence upon which it relied in the proposal, and to evaluate additional information." *Id.* at 56,781. First, the agency explained, various commenters had demonstrated that the clinical studies cited as proof of the safety and effectiveness of CAB and polyacrylate-silicone lenses [4] then on the market did not, after all, add up to "valid scientific evidence." *Id.* at 56,780. Second, even if the studies did constitute such evidence, they were "insufficient to justify reclassification" because they "fail[ed] to establish the safety and effectiveness of [RGP] lenses as a generic type of device." *Id.* Given the countless conceivable combinations of "polymer formulation and manufacturing processes," and the corresponding variations in lenses' "nontoxicity, biocompatibility, [and] light transmission," the FDA could not conclude that mere membership in the family of "RGP lenses" clinched any particular lens' safety and effectiveness. *Id.*

The FDA thus determined that no reclassification of RGP lenses could provide reasonable assurance of safety and effectiveness: class I status was not feasible because the FDA could not determine whether a new lens was "substantially equivalent" to an already-marketed lens without securing a wealth of detailed information about both lenses' composition and manufacture; and class II status was not in order because, even if such information could be gathered for the purpose of establishing a "performance standard" and measuring new lenses against it, conformity with the standard would not guarantee that a lens would function safely and effectively in the human eye. *Id.* at 56,780-81. "In short, FDA learned that at this stage in [RGP lens] development, there is no

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[4] The petition for review concerns only the FDA's treatment of polyacrylate-silicone lenses. Brief of Petitioner at 8 n.4. Accordingly, the term "RGP lenses," as henceforth used in this opinion, denotes lenses made of polyacrylate-silicone.

substitute for clinical trials [i.e., class III status] to provide reasonable assurance of the safety and effectiveness of these lenses." *Id.* at 56,781.

CLMA complains, in petitioning for review, that the FDA has disregarded a medical consensus favoring reclassification and has rendered insensible the requirement of "valid scientific evidence." We recognize substantial merit in CLMA's argument that RGP lenses should not be locked within so tight a regulatory regime. Nonetheless, we cannot disturb the FDA's decision. The agency acted within an area of its expertise, it ruled in a manner at least arguably consistent with the statutory scheme, and it considered the matter in a detailed, adequately reasoned fashion. We therefore defer to the agency and affirm its judgment. *See Chevron, U.S.A., Inc. v. Natural Resources Defense Council*, 104 S. Ct. 2778, 2782-83 (1984); *Rettig v. Pension Benefit Guaranty Corp.*, 744 F.2d 133, 151 (D.C. Cir. 1984) (quoting *Chevron*).

II.

We address at the outset CLMA arguments that the entire reclassification project was misconceived because RGP lenses were never class III devices to begin with. FDA's responses [5] indicate, correctly as we see the regu-

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[5] The FDA initially asserts that we lack "jurisdiction" to consider these arguments "because CLMA did not raise them in the rulemaking proceeding." Brief for Respondent at 51. If the arguments were placed before the agency, however, we may review them even if CLMA was not the presenter. *See* Toy Mfrs. of Am. v. Consumer Prod. Safety Comm'n, 630 F.2d 70, 73 n.5 (2d Cir. 1980); *see also* Lorion v. United States NRC, 712 F.2d 1472, 1474 (D.C. Cir. 1983) (court reviews "only those contentions subjected to agency scrutiny during the administrative process"), *rev'd on other grounds sub nom.* Florida Power & Light Co. v. Lorion, 105 S. Ct. 1598 (1985). Inspection of the challenged withdrawal notice reveals that the arguments in question, or substantially similar ones, were in fact rehearsed before the agency.

latory scheme, the limitations of the categories Congress established.

First, CLMA maintains that RGP lenses are not properly drawn into the web of the Amendments' "transitional provisions." The provision in question assigns to class III "[a]ny device intended for human use . . . which the [FDA] in a notice published in the Federal Register before the enactment date has declared to be a new drug." 21 U.S.C. § 360j(*l*)(1)(E) (1982). The FDA identifies its September 1975 announcement of "Regulatory Policy and Proposed Rulemaking for Marketing Contact Lenses," *see supra* p. 5, as the relevant notice. CLMA characterizes that notice as a preliminary announcement, merely a proposal for a declaration of new drug status, not the declaration itself. Brief of Petitioner at 52.

The asserted distinction between declaration and proposed declaration, in the context of the Amendments, lacks persuasive force. The statute requires only notice—not, for example, notice tested in the crucible of public comment. Further, to the extent that CLMA's argument rests not on statutory interpretation but on construction of the September 1975 declaration as tentative, we cannot agree. The announcement conveys the distinct impression that regulation of non-PMMA lenses as "new drugs" was a fait accompli, at that stage missing only a formal seal:

> The policy of the [FDA] of regarding all contact lenses other than those consisting [almost] entirely of PMMA as new drugs has been publicized and is generally known to contact lens manufacturers. . . .
>
> . . . .
>
> Although the Agency's enforcement policy regarding contact lenses has previously been publicized, this policy is not set forth in Title 21 of the Code of Federal Regulations. Accordingly, the Commissioner of Food and Drugs has concluded that, for-

> mally to advise the public, this regulatory policy should be promulgated as a regulation and codified in Title 21, C.F.R.

New Drug Notice, 40 Fed. Reg. at 44,845.[6]

Second, CLMA contends that RGP lenses are "custom devices" as that term is defined in the Amendments, and are on that account exempt from the classification scheme. A "custom device" is

> any device which, in order to comply with the order of an individual physician or dentist . . . necessarily deviates from an otherwise applicable performance standard or [premarket approval] requirement . . . if (1) the device is not generally available in finished

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[6] CLMA also suggests that the September 1975 announcement was inadequate in that it "did not mention polyacrylate-silicone lenses. The only polymers specifically mentioned were CAB . . . , polycarbonate, silicone, and HEMA, types of contact lenses which are readily distinguishable from polyacrylate silicone." Brief of Petitioner at 53. But the list to which CLMA refers did not purport to be exclusive. It merely cited examples of contact lens materials about whose safety and effectiveness the FDA was particularly concerned—materials "other than PMMA." New Drug Notice, 40 Fed. Reg. at 44,845. Polyacrylate-silicone, CLMA does not deny, is a further example of such material.

Our view that RGP lenses were covered by the September 1975 announcement, and are therefore properly ranked as class III devices under the Amendments' transitional provisions, suffices to answer CLMA's further contention that these lenses merit less stringent regulation because of their "substantial equivalen[ce]" to PMMA lenses. *See* Brief of Petitioner at 61-63. The 1975 announcement, and subsequent FDA glosses on it, foreclose any argument that RGP lenses and lenses made almost entirely of PMMA instance the same "type of device"; thus, there is no occasion for a substantial-equivalence determination. *See* 21 U.S.C. § 360c(f)(1)(A) (1982); *cf.* 21 C.F.R. § 860.84 (1984) (distinguishing, for classification purposes, between (1) devices substantially equivalent to pre-Amendments devices, and (2) devices regulated as "new drugs").

> form for purchase or for dispensing upon prescription and is not offered through labeling or advertising by the manufacturer, importer, or distributor thereof for commercial distribution, and (2) such device—
>
> > (A) (i) is intended for use by an individual patient named in such order of such physician or dentist . . . and is to be made in a specific form for such patient, [and]
> >
> > . . .
> >
> > (B) is not generally available to or generally used by other physicians or dentists . . . .

21 U.S.C. § 360j(b) (1982). The definition is an eyeful, but essentially it appears to reflect a commonsense congressional judgment that the design and composition of certain medical devices are so individualized that subjecting them to the usual regulatory controls would be impractical (and a complementary judgment that such particularly constructed devices are so closely monitored by the prescribing physician that stringent regulation might well be excessive). The House Report on the Amendments lists as examples of custom devices "orthopedic and other prosthetic devices, dental devices, and specially-designed orthopedic footwear"; the same report cautions that invocation of the exemption must be "limited." HOUSE REPORT, *supra* p. 3, at 44.

We are satisfied that the FDA acted reasonably in refusing to accord custom-device status to RGP lenses. It suffices to observe that the FDA could rationally regard such lenses as "generally available to or generally used by other physicians." CLMA's argument to the contrary focuses obsessively on the individual lens ground to a particular doctor's specifications; CLMA disregards the consideration, urged by the FDA, that the statutory language is most sensibly read as referring to a more or less inclusive class of devices rather than to any given exemplar of the class. And even if the relevant question

were whether a specifically prescribed lens was "generally available to or generally used by other physicians," there would be force to the FDA's contention that any specimen lens "is merely a variation within an approved range of powers and anterior and posterior surface contours." Brief for Respondent at 62. In other words, prescriptions for all but the most pathological eyes are likely to be replicated again and again and thus to be "generally used." CLMA insists that this construction of "generally used" could as easily lead to a ruling that orthopedic shoes are not "custom devices." But insofar as the FDA's conclusion from the logic and language of the statute appears contrary to the result intimated by some of the examples of "custom devices" offered in the legislative history, the FDA has properly cast its lot with the former. *See, e.g., Eagle-Picher Industries v. United States EPA*, 759 F.2d 922, 929 (D.C. Cir. 1985).

In short, it appears to us from the arguments made that the premise on which the FDA's initial reclassification proposal rested—that RGP lenses are currently class III devices—is altogether reasonable. The critical question that remains is whether the FDA could rationally refuse to bring its reclassification proposal to fruition.

III.

The FDA has consistently maintained that proponents of reclassification assume the burden of demonstrating—through "publicly available, valid scientific evidence"—that the device's present classification is inappropriate and that the proposed classification will provide reasonable assurance of the device's safety and effectiveness. *See, e.g.*, 48 Fed. Reg. at 56,779. We cannot fault the FDA's assignment of the burden of proof to those seeking to change the status quo. *See, e.g.*, HOUSE REPORT, *supra* p. 3, at 40. Thus, CLMA's claim that maintenance of class III status for RGP lenses lacks record support,

even if true, is off target. More to the point, CLMA asserts that the FDA in these proceedings has adopted an unreasonably strict view of what constitutes "valid scientific evidence." Though CLMA presses this argument with vigor, we are mindful that in such matters generalist courts see through a glass darkly and should be especially reluctant to upset an expert agency's judgment that a party has *failed* to adduce sufficient scientific proof of safety and effectiveness.

The FDA's rationale for withdrawing its reclassification proposal opens with the rather belated assertion that nothing in the record establishes the safety and effectiveness of RGP lenses now on the market. Facets of this position are unsettling. In justification of its current stance, the FDA disparaged, *see* 48 Fed. Reg. at 56,784-85, the same studies it had once acclaimed, *see* Reclassification Proposal, 47 Fed. Reg. at 53,406-09, and retracted, *see* 48 Fed. Reg. at 56,783, its earlier assertion that "[t]he safety of the device also is shown by the absence of reports in the literature of serious, irreversible adverse effects on health presented by the device," *see* Reclassification Proposal, 47 Fed. Reg. at 53,405. But the reclassification proposal specifically asked for comment on whether "the data . . . constitute sufficient 'valid scientific evidence.'" *Id.* at 53,410. We would be denying the value of notice-and-comment rulemaking were we to condemn the FDA for altering its outlook on the basis of submissions it received.

Citing its regulation declaring that "[i]solated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness," 21 C.F.R. § 860.7(c)(2) (1984), the FDA discounted the praises sung by dozens of "contact lens professionals" who favored reclassification and who reported that none of their patients had ever experienced serious problems with RGP lenses. 48 Fed.

Reg. at 56,786-87. We find the FDA's categorical belittlement of these eyewitness comments somewhat numbing, but we cannot gainsay the FDA's judgment that although such testimonials may suffice to *disprove* safety and effectiveness, they fail to establish with scientific rigor the absence of danger. *See* 21 C.F.R. § 860.7(c)(2).

The FDA's ultimate resistance to conceding the safety and effectiveness of lenses now on the market is perhaps most remarkable because these are the very lenses already granted premarket approval on the application of particular manufacturers. The agency's demand for compelling proof on matters presumably demonstrated to it convincingly by the licensed manufacturers, however, is a conundrum the statute itself sets up. Under the Amendments, trade secret information that a manufacturer submits to secure premarket approval may not be cited by the FDA or any third party in aid of reclassification proposals. 21 U.S.C. § 360j(c), (h)(3) (1982). Much as in patent law, Congress has determined that free riding is too high a price to pay for vigorous competition among medical device manufacturers;[7] the FDA is not at liberty to disregard this determination.

Of decisive importance, however, the FDA's refusal to reclassify RGP lenses does not stand or fall with the FDA's limited-purpose agnosticism about the safety and effectiveness of lenses currently on the market. Independently sufficient and far more persuasive is the FDA's

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[7] As the legislative history explains:

> To use trade secret information submitted in connection with a class III device as the basis for "downgrading" it into class II status—and thus allowing it to be replicated by competitors to conform to a standard—would destroy the originator's competitive advantage and could serve to stifle the initiative for innovation.

HOUSE REPORT, *supra* p. 3, at 50.

determination that all reclassification proposals to date "inadequately characterize" the class of RGP lenses. That is, even if the available evidence demonstrates the safety and effectiveness of lenses already on the market, this evidence cannot be taken as proof that any RGP lens a manufacturer might create will meet the statutory requirements; thus, at least for the present, the premarket approval process is unavoidable. "[T]he safety and effectiveness of a contact lens is a function of the complex interrelationship of material, design, and manufacture that results in a unique set of physical, chemical, mechanical, and optical characteristics." 48 Fed. Reg. at 56,792. Alter any one of these variables, the FDA now maintains, and you have a unique new lens whose safety and effectiveness are unknown and, without thorough clinical testing, unknowable. To be sure, the reclassification proposal described RGP lenses generically in glowing terms: "Contact lenses composed of . . . polyacrylate-silicone are characterized as chemically and physically stable under the conditions of their intended use, optically clear, nontoxic, and nonallergenic." Reclassification Proposal, 47 Fed. Reg. at 53,404. But in retrospective clarification, the FDA explains this statement as the depiction of a paradigm rather than an assertion that every potential combination of RGP materials, design, and manufacture will prove safe and effective.

The inadequacy of generic characterization of RGP lenses thus emerges as a mainstay of the FDA's contention that nothing short of lens-by-lens clinical testing and premarket approval will ensure safety and effectiveness. If RGP lenses were class I devices, the FDA would have no firmer basis on which to divine the safety and effectiveness of new lenses than a ninety-day inquiry into whether the lenses were "substantially equivalent" to other lenses already on the market. *See* 21 U.S.C. § 360(k), 360c(f)(1)(A) (1982); 21 C.F.R. § 807.87 (1984). In its reclassification proposal, the FDA asserted that such

an inquiry would suffice—provided, however, that the prospective manufacturer was

> prepared to demonstrate substantial equivalence in terms including, but not limited to, design; composition; optical transmission (and homogeneity) and index of refraction; and other physical properties including oxygen permeability, chemical and physical stability, tensile and flexural strength; biocompatibility, including cytotoxicity, eye irritation, and nonsupport of bacterial growth; impurities; leachables; heavy metal levels; preservative uptake and release; . . . lens care/cleaning regimen compatibility[; and manufacturing process].

Reclassification Proposal, 47 Fed. Reg. at 53,405.

The detail of this checklist suggests that, from the start, the FDA felt insecure about reclassifying RGP lenses. Upon withdrawing its proposal, the FDA announced its tardy recognition that the contemplated submission would be "indistinguishable" from the data required in a premarket approval application. 48 Fed. Reg. at 56,790. In other words, on close inspection, the FDA determined that class I assignment simply was not feasible. Given the detailed data submission necessary to find "substantial equivalence," prospective RGP lens manufacturers would be put to a burden approaching that entailed by the premarket approval process. At the same time, appraising such evidence "on a comparison basis" rather than for the purpose of "determin[ing] the safety and effectiveness of a device in the first instance," *id.*, would be both difficult and constraining. Not only would the problem of trade secret information, *see supra* p. 16, impede comparative evaluation; in addition, the exacting character of the comparisons involved might discourage innovation by requiring the manufacturer of a new RGP lens to demonstrate "substantial equivalence" almost to the point of patent infringement. *See, e.g.*,

Joint Appendix (J.A.) at 334 (comments of Dow Corning Ophthalmics).[8]

The FDA's doubts about generic characterization of RGP lenses led it to conclude as well that class II "performance standards," such as those formulated by the American National Standards Institute, would fail to provide reasonable assurance of safety and effectiveness. *See* 48 Fed. Reg. at 56,791. Although compliance with such standards may be easy to measure and may attest to a lens' physical, chemical, and optical integrity, the FDA observes that there is no scientifically proven relationship between fulfillment of the laboratory criteria and performance in the human eye.

On its face, the proposition that "minor changes in lens material formulation or manufacturing process can significantly [and unpredictably] affect the safety and effectiveness of lenses manufactured from the material," *id.* at 56,780, appears at least plausible. Indeed, a diluted form of this proposition—the chance that "there may conceivably be polymeric combinations within the category of polyacrylate-silicone which are not suitable for making RGP lenses"—strikes CLMA as "self-evident." Brief of Petitioner at 47. CLMA's complaint is that the imposition of expensive clinical testing requirements on each new type of RGP lens—requirements to which fewer than five percent of all medical devices are subject, *see id.* at 6 & n.3—is wholly out of proportion to the lenses' capacity for mischief.

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[8] In discussing the "substantially equivalent" test, the Amendments' legislative history confirms that the FDA is well within its discretion in declining to attempt comparison of devices that are disparate in such important respects as composition or design: "differences between 'new' and marketed devices in materials [or] design . . . would have a bearing on the adequacy of information as to a new device's safety and effectiveness, and such [new] devices should be automatically classified into class III." HOUSE REPORT, *supra* p. 3, at 36.

Given the record before the FDA, however, the agency could responsibly conclude that novel RGP lenses pose "a potential unreasonable risk of illness or injury." 21 U.S.C. § 360c(a)(1)(C) (1982) (describing conditions under which FDA may place pre-Amendments device in class III); *see, e.g.*, J.A. 339 (comments of David M. Worthen, M.D.); *id.* at 354, 357 (comments of Syntex Ophthalmics, Inc.); *id.* at 381 (comments of Barnes-Hind/Hydrocurve, Inc.); *see also* Brief for Respondent at 53-55 (arguing that, in any event, CLMA failed to demonstrate the nonexistence of such risk). It is true that companies like Syntex Ophthalmics, whose RGP lenses had already won premarket approval, were the principal doomsayers. But their apparent interest does not render their comment valueless. *See National Soft Drink Association v. Block*, 721 F.2d 1348, 1354 (D.C. Cir. 1983) ("We do not weigh the evidence; we merely examine the record to see if there is evidence, which if accepted by the Secretary, supports the determination of the agency.").[9]

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[9] CLMA further contends that the FDA abused its discretion by failing to consider the controlled clinical setting in which contact lenses are prescribed and fitted. The safety and effectiveness of a device are to be determined, in part, "with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device." 21 U.S.C. § 360c(a)(2)(B) (1982). CLMA argues that RGP lenses present no risk of irreversible injury; rather, the patient's eyes simply get a little red, at which point his optometrist or ophthalmologist orders a different sort of lens. Brief of Petitioner at 33; *see* Reply Brief of Petitioner at 12 (in this manner, competition will weed out unsafe and ineffective lenses without the need for FDA supervision).

The FDA usefully might have supplied a more explicit acknowledgment of the context in which RGP lenses are marketed, and a fuller explanation of why that context does not obviate the need for strict regulation. *Cf.* 48 Fed. Reg. at 56,787-88 (denying that medical supervision justifies enlargement of reclassification proposal to encompass nonspherical lens designs about whose safety and effectiveness there is

We are troubled, nonetheless, by the argument that the FDA's treatment of RGP lenses, even if internally logical and supported by several comments in the record, is impeached by the agency's action in other dockets. Comparative sideglances, CLMA contends, demonstrate graphically that RGP lenses have received an inordinately hard look. For example, in January 1982, the FDA proposed to classify 119 previously unclassified ophthalmic devices already on the market when Congress passed the Amendments; in that proposal, the FDA described "artificial eyes" generically as devices "usually made of glass or plastic," without any suggestion that a more precise specification of materials or manufacturing processes might be necessary. Mass Classification Proposal, 47 Fed. Reg. at 3724. It may make sense to say that devices designed for prolonged contact with so delicate and vital an organ as the living eye merit more circumspect regulation than do devices that merely stand in for that organ once it is lost; to the extent that this proposition is intuitively obvious, the FDA may be forgiven for not stating it. But how does the FDA account for its proposal, *id.* at 3736, to regulate PMMA lenses as class II devices? Is it not myopic for the FDA to ignore the variations in materials and manufacture of devices that appear to present risks of the same order as those posed by RGP lenses—devices that, in fact, raise the additional problem of depriving the cornea of oxygen?

The FDA implies that PMMA lenses' "extensive history of safe and effective human use" justifies a more lenient form of regulation. *See* 48 Fed. Reg. at 56,787.

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a "complete lack" of evidence). But CLMA's argument appears rooted in a premise the FDA has quite clearly rejected —that the risks posed by RGP lenses are too inconsequential to merit prior regulatory restraints. And surely the infamous histories of the two devices that principally inspired the Amendments, *see supra* p. 2, belie the assertion that the participation of a doctor renders premarket approval unnecessary.

This response is not altogether satisfactory. Although an "extensive history of safe and effective human use" may constitute, or obviate the need for, "valid scientific evidence" of the safety and effectiveness of PMMA lenses currently on the market,[10] it cannot—by the FDA's own hypothesis—inform us about lenses that as yet are but a glimmer in a polymer chemist's eye. Perhaps the range of possibilities is narrower, the predictability of results greater, for PMMA lenses than for RGP lenses. *Cf.* 48 Fed. Reg. at 56,787 (suggesting "potential significant differences in . . . uniformity" between PMMA and RGP lenses). If not, we would be hard-pressed to reconcile differential classification of the two devices. *See also* J.A. 388 (comments of Precision-Cosmet Co.) (criticizing "the 'hard lens attitude' in the industry which is essentially [that] one will do just as one pleases, since 'hard' lenses have never hurt anyone").

But the issue is not ripe for our consideration. The FDA acts on classification initiatives at a pace fairly

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[10] In its proposal to classify 119 ophthalmic devices, for instance, the FDA validated its advisory panel's reliance on essentially anecdotal evidence:

> In many cases, the Panel based its recommendations on Panel members' personal knowledge of, and clinical experience with, the devices under review. The Panel particularly relied upon clinical experience and judgment when considering a simple device that had been used extensively and was accepted widely before the amendments were enacted. . . . FDA has determined that clinical experience and judgment is valid scientific evidence for classifying certain devices.

Mass Classification Proposal, 47 Fed. Reg. at 3696. The panel's recommendation regarding PMMA lenses seems to have been based on the same sort of evidence. *See id.* at 3736. By the year 2000, therefore, if the FDA follows a consistent course, we would expect questions about the safety and effectiveness of lenses already on the market, *see supra* pp. 15-16, to pose no continuing impediment to reclassification of RGP lenses.

described as glacial. The January 1982 proposal to place PMMA lenses in class II remains only a proposal. Since that proposal antedates by almost two years the CLMA-challenged withdrawal of the proposed reclassification of RGP lenses, we would not be surprised if the FDA were having second thoughts. We do not prejudge the appropriate classification of PMMA lenses; we suggest only that, should the FDA ultimately decide to treat PMMA and RGP lenses differently, we will not feel that our respect for the agency's judgment has been vindicated unless the FDA explains why such a distinction is coherent. In the meantime PMMA lenses continue to be entirely free of any classification, but that is the way the statute Congress designed works.

IV.

We are cognizant of the ironies effected by the statute and the FDA's initially insecure administration of it. Considering the difficulty of the assignment Congress entrusted to the agency, and the respect we owe to the FDA's expert judgment, however, we cannot say that the action we have been asked to review is unlawful. Many of CLMA's claims of inequitable treatment are better addressed to Congress; others are not yet ripe. We hold simply and only that at this juncture, the FDA has not been shown to have proceeded without reason or regard for the statute in withdrawing its proposal to reclassify RGP lenses. The petition for review is accordingly dismissed and the challenged decision is

Affirmed.

APPENDIX C

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

SEPTEMBER TERM, 1984

No. 84-1025

CONTACT LENS MANUFACTURERS ASSOCIATION

v.

FOOD AND DRUG ADMINISTRATION OF THE
DEPARTMENT OF HEALTH AND HUMAN SERVICES

[Filed September 10, 1985. George A. Fisher, Clerk]

ORDER

Upon consideration of petitioner's petition for rehearing, it is

ORDERED, by the Court, that the petition is denied.

Per Curiam

FOR THE COURT
GEORGE A. FISHER, CLERK

By: /s/ ROBERT A. BONNER
Robert A. Bonner
Chief Deputy Clerk

APPENDIX D

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

21 CFR PART 886

[Docket No. 82N-0180]

RECLASSIFICATION OF DAILY WEAR SPHERICAL CONTACT LENSES CONSISTING OF RIGID GAS PERMEABLE MATERIALS; WITHDRAWAL OF PROPOSED RULE

AGENCY: Food and Drug Administration.

ACTION: Withdrawal of proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing its proposed rule to reclassify marketed daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials from class III (premarket approval) into class I (general controls). FDA has determined, after providing two opportunities for submission of comments and evidence, after holding a public hearing followed by an additional period for submission of comments and evidence, and after reconsidering the basis for FDA's tentative conclusion that class I would provide reasonable assurance of the safety and effectiveness of the device, that there is insufficient new, publicly available, valid scientific evidence to show that the device is safe and effective, to characterize the device adequately for the purpose of reclassification, or to demonstrate that either class I or class II (performance standards) would provide reasonable assurance of the safety and effectiveness of the device. Class III is necessary to provide such assurance.

EFFECTIVE DATE: *(Insert date of publication in the FEDERAL REGISTER.)*

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

For the convenience of the reader, the following is an index of the sections throughout this document:

I. History of the Proceedings.

II. Overview of the Basis for FDA's Decision.

- A. Background.
- B. Insufficient Evidence of Safety and Effectiveness.
- C. Inadequate Characterization of Materials.
- D. Inadequacy of Class I or Class II to Provide Reasonable Assurance of Safety and Effectiveness.
- E. Need for Clinical Trials.
- F. Conclusion.

III. Analysis of Comments.

- A. Classification.
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- C. Adequacy of Safety and Effectiveness Data.
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- G. Need for Clinical Trials.
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IV. References.

I. HISTORY OF THE PROCEEDINGS

In the FEDERAL REGISTER of November 26, 1982 (47 FR 53402), FDA published a proposed rule to reclassify marketed daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials from class III into class I. (For convenience, the lenses proposed for reclassification are referred to throughout this document as rigid gas permeable lenses and all other references to lenses refer to contact lenses.) Interested persons were given until December 27, 1982, to comment on the proposal. In the FEDERAL REGISTER of December 10, 1982 (47 FR 55497), FDA extended the comment period to January 26, 1983. Following a review of the comments received during this period, FDA determined that resolution of complex scientific issues raised by the comments would be facilitated by reopening the comment period to receive additional information on certain specific issues. Therefore, in the FEDERAL REGISTER of April 15, 1983 (48 FR 16293), FDA reopened the comment period for 30 days. Several requests for a public hearing before the Commissioner of Food and Drugs were received. In the FEDERAL REGISTER of April 26, 1983 (48 FR 18836), FDA announced that a public hearing would be held to afford interested persons an opportunity to present information and views on the issues involved in the reclassification proceeding. The hearing, which was held on May 26, 1983, was followed by an additional 15-day comment period to allow interested persons to submit written comments on matters raised at the hearing. The comment period following the hearing closed on June 10, 1983.

II. OVERVIEW OF THE BASIS FOR FDA'S DECISION

A. Background

Section 513(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(e)) authorizes FDA to reclassify a device based on "new information" respecting the device. (See the preamble to the proposed rule (47 FR 53404) for a comprehensive discussion of the meaning of the term "new information.") The "new information" on which any reclassification of a device is based is required to consist of "valid scientific evidence," as defined in § 860.7 of the regulations governing medical device classification procedures (21 CFR 860.7). FDA relies only upon such evidence to determine whether there is reasonable assurance that a device is safe and effective (§ 860.7(c)(1)). As the agency explained in the preamble to the final rule establishing Part 860 (21 CFR Part 860), the purpose of the Medical Device Amendments of 1976 (Pub. L. 94-295) (the amendments) is to assure the safety and effectiveness of medical devices intended for human use and such assurance necessarily demands a high standard of proof (43 FR 32988; July 28. 1978).

For the purpose of reclassification, the valid scientific evidence upon which the agency relies is required to be publicly available, i.e., may not be based on trade secret or confidential commercial information in any premarket approval application (PMA) for a medical device or on trade secret or confidential commercial information from any investigation concerning the safety and effectiveness of a device (section 520(c) of the act (21 U.S.C. 360j(c)). Such valid scientific evidence also may not be based upon the detailed summary of information respecting the safety and effectiveness of any device for which there is an approved PMA (section 520(h)(3) of the act) and which FDA is required to make available to the public upon issuance of an order approving a PMA (section 520(h)(1) of the act).

In the preamble to the proposed rule (47 FR 53404), FDA stated:

> To reclassify a device under section 513(e) of the act, the statute and the regulations require that the new, publicly available, valid scientific evidence of safety and effectiveness show (1) why the device should not remain in its present classification and (2) that the proposed reclassification will provide reasonable assurance of the safety and effectiveness of the device. In the case of a device classified in class III and proposed for reclassification into class I, the statute and the regulations require such evidence of safety and effectiveness to show (1) why the device should not remain in class III and (2) that general controls will provide reasonable assurance of the safety and effectiveness of the device.

The general controls are those authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration, listing, and premarket notification), 516 (banned devices), 518 (notification and other remedies), 519 (records and reports), and 520 (general provisions including current good manufacturing practice requirements) of the act (21 U.S.C. 351, 352, 360, 360f, 360h, 350i, and 360j).

In the preamble to the proposed rule, FDA summarized the data on which the proposed reclassification was based (47 FR 53406-53409) and tentatively concluded that rigid gas permeable lenses should be reclassified into class I, rather than into class II upon the effective date of a performance standard established under section 514 of the act (21 U.S.C. 360d) (47 FR 53404). In FDA's judgment at that time, the information discussed in the preamble showed that the device was safe and effective for its intended use. FDA also believed that the general controls provisions of the act would be sufficient to provide reasonable assurance of the safety and effectiveness of the device. The decision

to propose reclassification into class I, rather than class II once a performance standard was established, was based on FDA's belief that although sufficient information existed to establish a standard to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses, there was no need to establish a performance standard to provide such assurance.

Issuance of a proposed rule to reclassify a device from class III into class I under section 513(e) of the act does not preclude promulgation of a final rule to reclassify the device into class II, if the evidence warrants such action, particularly where, as in this proceeding, the preamble to the proposed rule invited comments on the appropriateness of reclassification into class II, before or after the establishment of a performance standard under section 514 of the act for the device. A class II device is one for which general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device. for which there is sufficient information to establish a performance standard to provide such assurance, and for which "it is therefore necessary to establish • • • a performance standard under section 514 to provide reasonable assurance of its safety and effectiveness" (section 513(a)(1)(B) of the act; 21 CFR 860.3(c)(2)).

In the preamble to the proposed rule (47 FR 53410), FDA invited comments on several specific issues including the following questions:

> 1. Do the data presented in this proposal constitute sufficient "valid scientific evidence" of safety and effectiveness to support reclassification of each marketed lens consisting of CAB or polyacrylate-silicone?
>
> a. If not, what additional publicly available data are there to support reclassification?
>
> b. If so, are general controls sufficient to provide reasonable assurance of the safety and effectiveness of the device?

c. If general controls are not sufficient to provide reasonable assurance of the safety and effectiveness of the device, is there sufficient information to establish a performance standard to provide such assurance?

d. If general controls are not sufficient, and there is sufficient information to establish a performance standard to provide reasonable assurance of [the] safety and effectiveness of the device, is a performance standard necessary to assure any of the lens properties or design characteristics that FDA has identified as "clinically significant" * * * or to protect against any of the concerns raised in the 1975 notice declaring as new drugs all contact lenses consisting of polymers other than PMMA * * *?

e. Should any reclassification take effect (i) before or (ii) after such a standard has been established?

* * * * *

3. With respect to the lenses proposed for reclassification, FDA has limited data on their use for the correction of hyperopia and in some cases aphakia. May FDA reclassify a lens for use in the correction of myopia, hyperopia, and aphakia based solely or primarily on data showing that the lens is safe and effective (a) for the correction of myopia? (b) for the correction of myopia and aphakia?

4. Does specifying the materials of which the lenses proposed for reclassification are principally composed adequately identify the lenses for the purpose of reclassification?

5. * * *, [T]he safety or effectiveness of a specific rigid gas permeable contact lens is affected by its specific composition, design, and various other clinically significant properties.

a. Do the data presented in this proposal provide sufficient "valid scientific evidence" of the safety and effectiveness of CAB or polyacrylate-silicone lenses of any specific composition, design, or other characteristic?

b. If the data do not provide this evidence, may the identified lenses be reclassified because of FDA's tentative decision that the safety and effectiveness of composition, design, or other clinically significant properties of specific lenses can be assured through premarket notification submissions and substantial equivalence determinations?

• • •

B. Insufficient Evidence of Safety and Effectiveness

In response to question 1 above, a number of comments presented cogent arguments that the data described in the preamble to the proposal do not constitute sufficient new, publicly available, valid scientific evidence (valid scientific evidence) of safety and effectiveness to support reclassification. FDA agrees in general with these comments, which are discussed in detail in section III.C. of this document. Additional comments in response to question 1.a. and in response to the April 15, 1983 notice reopening the comment period, in an effort to supply the valid scientific evidence of safety and effectiveness required for reclassification, submitted detailed summaries of a portion of clinical trials conducted on two specific polyacrylate-silicone contact lenses, and a detailed summary of the preclinical evaluation of one of the lenses. (No data pertaining to the safety or effectiveness of cellulose acetate butyrate (CAB) rigid gas permeable lenses were provided in or submitted with any comments.) As discussed in paragraph 14 of this document, serious questions have been raised concerning the completeness of the submitted data. Even if there were no such questions, however, the data merely would serve to show the safety and effectiveness of two polyacrylate-

silicone lenses characterized only by brand name and made of unspecified material. Such a showing would be insufficient to justify reclassification because, among other things, the information would fail to establish the safety and effectiveness of polyacrylate-silicone lenses as a generic type of device.

C. Inadequate Characterization of Materials

CAB or polyacrylate-silicone materials that might be used for manufacturing rigid gas permeable lenses can consist of thousands of formulations and have a wide variety of physical and chemical properties. Only a small percentage of such materials have the necessary combination of characteristics of nontoxicity, biocompatibility, light transmission, and machinability to serve as the basis for the design and manufacture of safe and effective contact lenses. Comments from opponents of reclassification argue, and a comment from one proponent of reclassification agrees, that minor changes in lens material formulation or manufacturing process can significantly affect the safety and effectiveness of lenses manufactured from the material. A comment opposing reclassification further argues that although controlled minor changes in a single variable by a manufacturer can result in predictable changes in safety and effectiveness, major or multiple changes, or a change from one manufacturer to another, can result in changes in the lens' clinical performance that are not easily predicted.

FDA agrees with the comments opposing reclassification. If specific CAB or polyacrylate-silicone lenses had been shown to be safe and effective by valid scientific evidence and had been characterized by polymer formulation and manufacturing processes, such information might have been sufficient to have allowed comparison, for the purpose of determining substantive equivalence, with other lenses that had been shown to be very similar in polymer formulation and manufacturing process, and, as a result, to have al-

lowed an inference of comparable safety and effectiveness of such other lenses. However, no information about polymer formulation and no information about manufacturing processes was disclosed in or submitted with any of the comments, and FDA is prohibited by sections 301(j) and 520(c) of the act (21 U.S.C. 331(j) and 360j(c)) from disclosing such information from PMA's or files for investigational devices under development pursuant to an investigational device exemption (IDE) because such information constitutes trade secret data. Lacking information about polymer formulation and manufacturing processes, it is not possible to compare one rigid gas permeable lens to another for the purpose of determining substantial equivalence; individual CAB and polyacrylate-silicone lenses are sufficiently different from one another that the fact that they are made from CAB or polyacrylate-silicone does not allow an inference of comparable safety and effectiveness.

In summary, clinical evidence of the safety and effectiveness of a limited number of individual lenses, characterized only by general family of material, i.e., CAB or polyacrylate-silicone, brand name, and manufacturer, would be insufficient to serve as a basis for reclassification of a generic type of device.

D. Inadequacy of Class I or Class II to Provide Reasonable Assurance of Safety and Effectiveness

Two comments from proponents of reclassification argue in response to questions 1.b. and 5.b. above that the safety and effectiveness of polyacrylate-silicone lenses, as identified in a definition offered by both comments, can be evaluated against a group of parameters with assigned acceptance limits that are proposed in these comments as criteria for the determination of substantial equivalence after the reclassification of such lenses into class I. These parameters include certain physical, optical, chemical, toxicological, and biocompatibility criteria, but exclude clinical evaluation. The comments argue that lenses that met the assigned

limits for the parameters would be safe and effective, which would negate the need for clinical trials as well as the need for identification of the lenses with detailed information on polymer formulation and manufacturing processes. The comments accordingly argue that the absence of information concerning formulation and processing is not a bar to reclassification. The comments further argue that use of these parameters would allow FDA to determine substantial equivalence of new lenses to reclassified lenses and would ensure the adequacy of FDA review of premarket notification submissions to screen out unsafe or ineffective lenses. Other comments argue that to establish such parameters as criteria for determining substantial equivalence to a class I device would be de facto imposition of a performance standard. These comments urge the agency to use such parameters as the basis for the development of a performance standard under section 514 of the act, and to reclassify the lenses into class II.

To suffice as a basis for reclassification into class I or class II, such a group of parameters, whether used to determine substantial equivalence or as the basis for a performance standard, would of necessity have to be shown capable of providing reasonable assurance of safety and effectiveness of the lenses by valid scientific evidence. No comments contained, and FDA is unaware of, any evidence that if a lens met these parameters, there would be reasonable assurance that the lens was safe and effective, or in the event of reclassification, that the lens would be substantially equivalent in terms of safety and effectiveness to any lens that had been reclassified. The absence of the requisite evidence precludes using the parameters offered by the comments as a basis for reclassification of rigid gas permeable lenses into class I or class II.

E. Need for Clinical Trials

Several comments argue that the results of nonclinical laboratory studies cannot be used to predict the clinical

performance of a contact lens. Other comments argue that the clinical performance of a contact lens can be readily predicted from nonclinical laboratory studies.

None of the comments submitted any data to support their arguments. FDA is unaware of any combination of nonclinical laboratory studies capable of predicting the clinical performance of any contact lens on the human eye. Such studies serve well to screen out materials that should not go on to clinical trials. For example, in vitro or animal toxicity tests of a material or a material extract may reveal an overt cytotoxic effect to an undifferentiated cell line (the correlation of this effect to an ocular response in humans has not been established) or gross systemic or ocular toxicity. These tests are presumptive in nature and serve at best to provide reasonable assurance that subjects in a clinical trial would not be placed at undue risk from exposure to a new or modified material used to make a contact lens. However, nonclinical laboratory studies cannot provide any data on human ocular biocompatibility, or on adequacy of design (e.g., weight, thickness, geometry, centration), comfort, stability, durability, fit, and visual acuity, nor can the results of such studies be used as the sole basis from which to predict the clinical performance of an approved contact lens for which approval for a new indication is sought.

FDA believes that the safety and effectiveness of a contact lens is a function of the complex interrelationship of material, design, and manufacture that results in a unique set of physical, chemical, mechanical, and optical characteristics. When prescribed and fitted properly, a lens with this unique set of characteristics should provide safe and effective visual correction in a human eye with a specific diagnosed ametropia. FDA believes that contact lenses made from a new material, including material that has been significantly modified, contact lenses made to significantly modified designs, and contact lenses for which

approval for a new indication is sought, cannot at this time be shown to be safe and effective without clinical, as well as preclinical, evaluation.

F. Conclusion

FDA has carefully reviewed and analyzed all the comments received as well as the oral and written testimony presented at the public hearing and has further reviewed the data discussed in the preamble to the proposed rule. On the basis of all this information, FDA has concluded, contrary to the tentative conclusions stated in the proposal, that there is insufficient valid scientific evidence to show that the rigid gas permeable lenses proposed for reclassification are safe and effective, to characterize the device adequately for the purpose of reclassification, or to demonstrate that either class I or class II would provide reasonable assurance of the safety and effectiveness of the device. Class III is still necessary to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses.

This document withdraws FDA's first proposal to reclassify a device under section 513(e) of the act. The agency initiated this proceeding because it tentatively concluded that the new, publicly available, valid scientific evidence of safety and effectiveness it had gathered was sufficient to show that rigid gas permeable lenses should not remain in class III and that class I would provide reasonable assurance of the safety and effectiveness of the lenses. However, as shown by the specific issues raised in the preamble to the proposed rule (47 FR 53410), the April 15, 1983 notice reopening the record, and the agency's decision to hold a public hearing on the proceeding (see 48 FR 18836), FDA was concerned about the sufficiency of the evidence it relied on in the proposal, and promulgation of a final rule reclassifying the lenses was far from certain. In response to the notice-and-comment procedures man-

dated by the act and the regulations, as well as the public hearing on the proposal, FDA received comments and oral and written testimony that required it to reevaluate the evidence upon which it relied in the proposal, and to evaluate additional information presented by interested persons. As a result of its evaluation and reevaluation of all the information in the record of this proceeding, FDA learned that the safety and effectiveness data summarized in the preamble to the proposal were seriously deficient in many respects, that lenses made of CAB or polyacrylate-silicone are the products of complex polymer formulation and manufacturing processes, that the information it would have to require in a premarket notification submission to determine whether a new lens is substantially equivalent to a reclassified lens would exceed the authority of section 510(k) of the act and Subpart E of Part 807 of the regulations governing premarket notification procedures (21 CFR Part 807, Subpart E), and that there is not sufficient valid scientific evidence to develop a performance standard under section 514 of the act to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses. In short, FDA learned that at this stage in their development, there is no substitute for clinical trials to provide reasonable assurance of the safety and effectiveness of these lenses.

III. ANALYSIS OF COMMENTS

The agency received approximately 200 comments on the proposal, including written and oral testimony presented at the May 26, 1983 public hearing. Comments were received from manufacturers of contact lenses and contact lens materials, optical laboratories, clinical investigators of contact lenses, industry associations, members of Congress, and other interested persons. The following is a summary of the significant comments received and FDA's responses to them.

A. Classification

1. One comment suggests that rigid gas permeable lenses are not class III devices under section 520(l)(1)(E) of the act. According to the comment, the notice published in the FEDERAL REGISTER of September 30, 1975 (40 FR 44844), which declared as new drugs contact lenses consisting of polymers other than polymethylmethacrylate (PMMA), was principally concerned with hydroxyethylmethacrylate (HEMA) contact lenses and was grounded on incorrect information as to the composition of then marketed PMMA lenses. The comment points out that then marketed PMMA lenses did not consist "entirely" of PMMA, citing the preamble to the proposed rule (47 FR 53404). The comment then argues that if the September 30, 1975 notice, which included a proposed rule to codify the agency's position, had not been withdrawn by a notice published in the FEDERAL REGISTER of January 13, 1978 (43 FR 1966), literal application of the September 30, 1975 notice would have required FDA to regulate all contact lenses as new drugs before enactment of the amendments. The comment also argues that the September 30, 1975 notice, as allegedly interpreted by a notice published in the FEDERAL REGISTER of December 16, 1977 (42 FR 63472) (the transitional notice) and the January 13, 1978 notice, applies only to HEMA (soft) lenses, and that rigid gas permeable lenses are more closely related to PMMA lenses than to soft lenses.

FDA disagrees with the comment. The term "soft" as used in reference to contact lenses in the September 30, 1975 notice, the transitional notice, and the January 13, 1978 notice encompasses all lenses other than those made of PMMA. That one or more of these notices used the term "soft contact lenses" as a synonym for "non-PMMA lenses" thus has no bearing on the classification of lenses consisting of polymers other than PMMA. Furthermore, the September 30, 1975 notice, which made it plain that

FDA had in the past regarded, and would continue to regard, as new drugs, contact lenses consisting of polymers other than PMMA, expressly cited CAB, polycarbonate, and silicone as examples of such other polymers (40 FR 44845). The notice, which advised that the agency had taken this position since the 1960's, accordingly applies to rigid gas permeable as well as soft lenses.

As a result of the September 30, 1975 declaration, under section 520(l)(1)(E) and (l)(3)(D)(i) of the act, non-PMMA contact lenses on the date of enactment of the amendments (the enactment date) were automatically classified into class III without need for regulations or other action on the part of the agency. The transitional notice and the January 13, 1978 notice, which withdrew the 1975 proposed rule but did not affect its declaration, simply provided interested persons further notice that non-PMMA lenses were class III devices subject to the premarket approval requirements of section 515 of the act (21 U.S.C. 360e).

Although the September 30, 1975 notice stated that FDA had in the past regarded, and would continue to regard, contact lenses consisting "entirely of PMMA" as devices, the notice stated: "[t]he Agency has undertaken a study to determine the extent to which adjuvants such as cross-linking agents, resin bases, catalysts, colorants, and anti-oxidants are used in the manufacture of contact lenses consisting of PMMA to determine the effects of such adjuvants on the essential physicochemical characteristics of PMMA and thus to determine which of these contact lenses may be regarded as devices and which should be regarded as new drugs" (40 FR 44845). The September 30, 1975 notice thus recognized that then marketed PMMA lenses did not consist "entirely" of PMMA, and "literal application" of the notice would not have required FDA to regulate all contact lenses as new drugs before enactment of the amendments.

FDA acknowledges that rigid gas permeable lenses are more closely related to PMMA lenses than to soft lenses. However, the components of rigid gas permeable lenses, e.g., CAB, silicone acrylate monomers, and derivatives of acrylate monomers, are not adjuvants. For this reason, as well as by the express terms of the September 30, 1975 notice, rigid gas permeable lenses are not PMMA lenses within the meaning of that notice.

FDA advises that any CAB lens for which a new drug application (NDA) was filed and no order of approval or refusal to approve had been issued on the enactment date, e.g., MESO Contact Lens, is a class III device under section 520(l)(1)(B) of the act; that any CAB lens for which a notice of claimed investigational exemption for a new drug (IND) was in effect on the enactment date, e.g., MESO Contact Lens, CABCURVE® Contact Lens, is a class III device under section 520(l)(1)(C) of the act; and that any CAB lens that is substantially equivalent to a CAB lens covered by section 520(l)(1)(B) or (C) is a class III device under section 520(l)(1)(D) of the act.

FDA advises that any polyacrylate-silicone lens for which an IND was in effect on the enactment date, e.g., POLYCON®, is a class III device under section 520(l)(1)(C) of the act and that any polyacrylate-silicone lens that is substantially equivalent to a polyacrylate-silicone lens covered by section 520(l)(1)(C) of the act is a class III device under section 520(l)(1)(D) of the act.

B. Identification

2. One comment argues that CAB and polyacrylate-silicone lenses constitute a generic type of device having essentially the same characteristics and that, under § 860.-120(b) of the regulations governing reclassification, any reclassification should extend to all devices falling within that generic type. The comment recommends that proposed § 886.5360 (21 CFR 886.5360) be amended to provide a

generic description of the device by eliminating the limitation to lenses in commercial distribution. Another comment argues that the proposed rule, which the comment characterizes as based on the composition of the device and its status as a contact lens subject to approved NDA's or PMA's, is unsound as a matter of policy and violates section 520(c) of the act. The comment points out that FDA, in the preamble to the proposed rule to classify ophthalmic devices, stated: "[i]t is not practical for FDA to publish an identification of each type of device that is so detailed as to anticipate every product feature that may be relevant in determining whether a new device is substantially equivalent to previous devices classified by regulation. * * *" (47 FR 3695; January 26, 1982). The comment claims that classification must reflect the potential risk of illness or injury and the need for varying levels of controls associated with the type or category of device rather than the specific device, and states that this focus on the type or category of device and the risks associated with such type or category has been FDA's previous approach to classification of all ophthalmic devices under the act and is required by the act. For these reasons, the comment requests that FDA withdraw proposed § 886.5360 and, if reclassification is deemed warranted, propose a classification of the category or type of device identified as "contact lenses."

FDA agrees that the identification paragraph of any classification regulation should provide a generic description of the device. As explained in sections II.B. and C. and paragraphs 13, 23, and 24 of this document, however, the lens proposed for reclassification—a daily wear spherical lens consisting of CAB or polyacrylate silicone—has not been adequately characterized for the purpose of reclassification. Accordingly, identification of the generic type of device as "the contact lens," or even "the rigid gas permeable lens," even broader identifications than included in the proposal, could not be adequate for that purpose. FDA notes that if the proposed rule had been revised and

promulgated to identify the generic type of device as "the rigid gas permeable lens," or as "the contact lens," and a manufacturer had submitted a premarket notification seeking to market a new lens, FDA, to determine whether the new lens was substantially equivalent to any lens in the generic type, still would have compared the new lens to lenses already covered by the final rule (see § 807.87(f) and (h) of the regulations governing premarket notification procedures).

FDA disagrees that identifying a device based on its composition or regulatory status violates the letter or the spirit of the act or the regulations issued under it. So long as there is sufficient valid scientific evidence showing (1) why a device should not remain in its present classification and (2) that a change in its classification will provide reasonable assurance of the safety and effectiveness of the device, nothing in section 520(c) of the act or any other section of the act, or in any of the regulations implementing any section of the act, precludes identifying the device by composition and previous status under section 505 (21 U.S.C. 355) or 515 of the act. FDA notes that the proposed rule to classify ophthalmic devices includes a proposal to classify into class II a device, namely, the PMMA contact lens, identified in part by composition (47 FR 3736).

C. Adequacy and Safety and Effectiveness Data

3. Several comments state that rigid gas permeable lenses may not be reclassified into a class other than class III unless there is adequate valid scientific evidence of safety and effectiveness to support reclassification.

FDA agrees with these comments (see the preamble to the proposed rule (47 FR 53404) and section II.A. of this document). Lacking adequate valid scientific evidence that rigid gas permeable lenses are safe and effective, and that class I would be sufficient to provide reasonable assurance of the safety and effectiveness of such lenses, FDA may not reclassify them from class III into class I or class II.

4. One comment states that the burden of proof that reclassification is appropriate is on FDA and on those who support reclassification, regardless of whether those opposing reclassification can or do submit evidence showing that reclassification is not appropriate.

FDA agrees with this comment. The legal standard for reclassification is set out in the preamble to the proposed rule (47 FR 53404) and in section II.A. of this document. FDA addressed the question of burden of proof in the April 15, 1983 notice reopening the comment period (48 FR 16293):

> FDA recognizes that to reclassify the contact lenses at issue in this rulemaking from class III into class I, it must have new, publicly available, valid scientific evidence of safety and effectiveness demonstrating why the lenses should not remain in class III and why the "general controls" authorized by the act will provide reasonable assurance of the safety and effectiveness of the lenses. * * * Although this notice requests specific evidence showing why the lenses should not be reclassified, as well as evidence showing why they should be reclassified, FDA has not shifted the burden of proof to those opposing reclassification.

5. Several comments argue that the evidence needed to reclassify a contact lens is at least equal to that which would be necessary to meet FDA's guideline concerning testing of contact lenses, "FDA Contact Lens Guidelines on Toxicology, Microbiology, Clinical Manufacturing Evaluation and Controls" (Ref. 5 of the proposal) (the contact lens guideline), and that FDA may not reclassify a lens proposed for reclassification unless the valid scientific evidence of the safety and effectiveness of that lens meets the criteria of the guideline.

FDA guidelines state procedures or standards of general applicability that are not legal requirements but are accept-

able to FDA for a subject matter which falls within the laws administered by the Commissioner (21 CFR 10.90(b)). Conformance to the contact lens guideline accordingly is not a legal prerequisite for premarket approval. It follows that conformance to the guideline is not a legal prerequisite for reclassification of contact lenses. The evidence of safety and effectiveness of the contact lenses proposed for reclassification has been evaluated by FDA against the criteria for valid scientific evidence specified in § 860.7 of the regulations.

FDA believes that the evidence needed to show that a rigid gas permeable lens is safe and effective for the purpose of reclassification is similar, but not necessarily identical to, the evidence suggested in the contact lens guideline to show safety and effectiveness for premarket approval. For example, for the purpose of reclassification, comprehensive clinical data combined with detailed information on polymer formulation and manufacturing processes might obviate the need for the detailed reporting of preclinical testing suggested in the guideline.

6. Several comments refer to FDA's statement in the preamble to the proposed rule that the safety of rigid gas permeable lenses is shown by the absence of reports in the literature of serious, irreversible adverse effects on health presented by the device, and the absence of such reports in FDA's Device Experience Network (DEN). The comments argue that rather than serving as evidence for reclassification of the device, the lack of evidence of such adverse effects is evidence of the success of the present class III classification in assuring that only safe and effective lenses are marketed. The comments further argue that extrapolation from the safety record of approved devices to that of future deregulated devices is inappropriate.

The comments do not accurately restate the preamble, which cited the absence of reports in the literature as one item of evidence of the safety of rigid gas permeable lenses

and simply noted that no serious, irreversible adverse effects on health presented by the device had been reported to DEN (47 FR 53405). FDA agrees, however, that the safety record of rigid gas permeable lenses to date represents the performance of lenses for which there are approved PMA's. The agency acknowledges that DEN is not comprehensive and advises that the mere absence of negative reports in this voluntary reporting system cannot establish the safety of a device. Before a device may be reclassified under section 513(e) of the act from class III into class I or class II, the act and the regulations require that the safety, as well as the effectiveness, of the device be established by valid scientific evidence.

7. A few comments suggest that FDA has not conducted an adequate search for evidence of serious or permanent injury from contact lens wear. One comment provided copies of published articles dealing with complications caused by certain silicone elastomer lenses marketed in Germany and Japan; other comments provided bibliographies of published articles dealing with injuries allegedly related to contact lens wear.

Before issuing the proposed rule, FDA searched diligently for evidence of serious, irreversible adverse effects presented by each of the lenses proposed for reclassification when used in accordance with its labeling and under proper professional supervision, and found no such evidence. Since then, FDA has reviewed articles cited in the comments as containing evidence of such effects. This latest review confirms FDA's earlier findings. Injuries to the eye related to use of approved contact lenses invariably are traceable to factors associated with improper lens use, care, or fitting. While such reports of injuries argue forcefully for the need for continued diligence in the regulation of contact lenses, they do not preclude reclassification if there is adequate, valid scientific evidence of the safety and effectiveness of the devices when used and fitted properly.

The silicone elastomer lenses associated with the reported complications in wearers of the lens in Germany and Japan were not, as admitted in the comment, of the type proposed for reclassification, and by definition would require premarket approval before being marketed in the United States.

8. One comment argues that safety and effectiveness data for contact lenses having different clinically significant properties and design characteristics cannot be pooled to show the safety and effectiveness of all lenses consisting of CAB or all lenses consisting of polyacrylate-silicone. The comment states that there are thousands of formulations of CAB which vary from one another in such significant characteristics as toxicity and dimensional stability. The comment concludes that generally accepted scientific methods for use of test results would dictate that data for lenses with differing safety and effectiveness parameters not be pooled.

FDA agrees with this comment. Data on the polymer formulation and manufacturing processes for the different approved CAB lenses are not publicly available. Unless the CAB lenses are shown to be identical by such data, the agency may only assume that each CAB lens has different safety and effectiveness parameters from other such lenses. In addition, pooling of the clinical safety and effectiveness data on which the proposed rule was based would be inappropriate because of the deficiencies in the data (see paragraphs 10 through 12 of this document). There is in the record no information identifying by polymer formulation, manufacturing process, and related parameters any of the rigid gas permeable lenses proposed for reclassification. Absent such information, the safety and effectiveness of one rigid gas permeable lens cannot be compared with the safety and effectiveness of another rigid gas permeable lens. This lack of characterizing data precludes pooling of data from clinical investigations.

9. In response to question 3 in the preamble to the proposed rule, two comments argue that any reclassification of rigid gas permeable lenses should include indications for the correction of hyperopia and aphakia as well as myopia because there appears to be no basis upon which to limit to specific refractive corrections the significance of the data presented in the preamble. Five comments argue on the contrary that data showing that a lens is safe and effective for myopia cannot be used to support the safety and effectiveness of the lens for the correction of hyperopia and aphakia. These comments state that lenses indicated for the correction of hyperopia and aphakia are of necessity significantly different in design and geometry from lenses indicated for the correction of myopia. These comments also state that lenses for the correction of hyperopia and aphakia generally require an increased lens center thickness compared to lenses for the correction of myopia. Increased lens center thickness results in a reduction in the oxygen permeability of the lens and concomitant safety and effectiveness concerns unique to these lenses, according to the comments. Therefore, the comments opposing reclassification conclude that only clinical trials can provide reasonable assurance of safety and effectiveness of a contact lens indicated for the correction of hyperopia or aphakia.

Because FDA is withdrawing the proposed rule, the question whether FDA may reclassify rigid gas permeable lenses for myopia, hyperopia, and aphakia based solely or primarily on data showing that the device is safe and effective for the correction of myopia, or myopia and aphakia, is moot. FDA advises, however, that none of the comments provide any evidence to support the contention that reclassification of rigid gas permeable lenses indicated for the correction of myopia, hyperopia, and aphakia could be based solely or primarily on data demonstrating that the lenses are safe and effective for the correction of myopia or for the correction of myopia and aphakia.

FDA agrees with the comments that argue that the lens characteristics required to provide safe and effective correction of hyperopia or aphakia are significantly different from the lens characteristics required to provide safe and effective correction of myopia. However, lenses indicated for the correction of hyperopia and aphakia may be identical in design and concomitant safety and effectiveness characteristics where the range of magnification for the two indications overlap. The aphakic eye is a worst case for both safety and effectiveness considerations for a contact lens because of physiological changes to the cornea from the insult of surgery. Among other things, these changes could result in alterations in corneal oxygen requirements. Consequently, FDA advises that for lenses identical in material, design, and magnification range, the safety and effectiveness of a lens for the correction of hyperopia may, in large measure, be inferred from evidence of the safety and effectiveness of a lens for the correction of aphakia. Similarly, if the safety and effectiveness concerns that are unique to a lens intended for the aphakic eye are adequately addressed by clinical trials of the lens in aphakic eyes, the safety and effectiveness of that lens may, in large measure, be inferred from evidence of its safety and effectiveness for the correction of hyperopia. FDA advises, however, that it has not been demonstrated by valid scientific evidence that the safety and effectiveness of a lens for the correction of hyperopia can be inferred solely from evidence of the safety and effectiveness of a lens for the correction of aphakia, or that the safety and effectiveness of a lens for the correction of aphakia can be inferred solely from evidence of the safety and effectiveness of a lens for the correction of hyperopia.

10. One comment generally criticizes the published articles (Refs. 22-27 (see 47 FR 53411)) relied on in the preamble to the proposed rule as valid scientific evidence of the safety and effectiveness of CAB lenses. The comment states that the articles are deficient in that they do not

consistently state clear objectives, that they do not have an adequate method of subject selection, that they do not include sufficient information to allow comparisons between test and control groups, and that most of the articles are based on retrospective clinical evaluation, and therefore suffer from the bias of evaluating successful patients. The comment states that none of the articles includes complete ocular data, and implies that the number of patients studied is inadequate.

FDA acknowledges that the articles criticized by the comment have some deficiencies in study protocols, in patient selection criteria, in the number of patients studied, or in reporting of important clinical results. FDA notes that no evidence of the safety or effectiveness of any CAB lens was included in or submitted with any comment on the proposed rule. Consequently, the deficiencies noted in the comment and which, as discussed below, show that the articles do not constitute valid scientific evidence of safety and effectiveness, preclude reclassification of CAB lenses.

a. *"A Clinical Study of CAB Lens Wear" by Kline and DeLuca (Ref. 22).* This study, which apparently was retrospective, reports on 100 myopic patients who could tolerate an unidentified CAB lens on an initial visit. The investigators' criteria for success were comfort, 8 hour wearing time, 20/25 visual acuity, and no adverse reactions. No data are provided on any of these criteria, nor is the period the patients were followed reported. Most of the article addresses fitting characteristics. FDA agrees with the comment that this study does not qualify as a controlled clinical investigation capable of demonstrating that the study lens is safe and effective for daily wear.

b. *"Clinical Experience with the Cabcurve Contact Lens" by Sigband (Ref. 23).* This study reports on 65 patients, including 54 myopes, 4 hyperopes, and 7 aphakes, who were "contact lens failures." The study includes no data on visual acuity, except a table of summarizing best

visual acuity achieved, and no data on any other evaluation criterion. The study population, which included only 55 successful patients, is small. However, the question of size is overshadowed by the absence of adequately reported data on any significant evaluation criterion.

c. *"Gas-Permeable Cellulose Acetate Butyrate (CAB) Contact Lens" by Hales (Ref. 24).* This study, which apparently is retrospective, reports on 50 patients who had been unsuccessful wearers of hard contact lenses and who were subsequently fitted with an unidentified CAB lens. The study contains one chart of visual acuity with CAB lenses as compared to visual acuity with hard lenses. No other data are provided. The small retrospectively reviewed patient population and the absence of data for any criterion except visual acuity renders this study inadequate to determine the safety and effectiveness of the lens under study.

d. *"Oxygen-Transmitting Hard Contact Lens" by Mandell (Ref. 25).* This study alludes to an experiment in which nine PMMA contact lens wearers were refitted with an unidentified CAB lens to determine whether the change would alleviate persistent edema associated with wearing the PMMA lenses. No data are provided on any criterion except edema. The study does not purport to establish the safety and effectiveness of lenses made of CAB.

e. *"Extended Wear of CAB Contact Lenses in Aphakic Patients" by Garcia (Ref. 26).* This study appears to be a well-conducted study of continuous extended wear (for 1 to 6 weeks between removals for cleaning) of a CAB lens for the treatment of aphakia. Patients were followed for an average of 24 months. However, the study's summary presentation of data does not allow scientific evaluation of the safety and effectiveness of the lens for continuous wear, or therefore, for daily wear. For example, the report contains no visual acuity data or quantitative data on edema, slit lamp findings, or epithelial staining, which are all necessary to permit scientific evaluation of the

safety and effectiveness of the lens. Because the study "lack[s] sufficient details to permit scientific evaluation," the study is "not regarded as valid scientific evidence to show safety or effectiveness" (21 CFR 860.7(c)(2)). The study lenses were identified as the Rynco Scientific Corp. Rx 56 Lens (used early in the study) and the Danker and Wohlk, Inc., Meso CAB lens (used late in the study).

f. *"Corneal Response to Extended Wear of CAB Contact Lenses in Aphakia" by Kaplan and Triber (Ref. 27).* The purpose of this study was to determine the effect of extended wear of Danker Labs., Inc., MESO CAB lenses on corneal thickness. The authors make no claim of establishing the safety or effectiveness of CAB lenses.

In conclusion, FDA agrees with the comment that Refs. 22-27 are inadequate to show the safety and effectiveness of CAB lenses.

11. A few comments state that the two published articles relied on in the preamble to the proposed rule ("Clinical Evaluation of the Polycon 8.5 Design" (Ref. 30) and "Patient Responses to Gas-Permeable Hard (Polycon) Contact Lenses" (Ref. 31); see 47 FR 53411) do not constitute adequate valid scientific evidence of the safety and effectiveness of the specific polyacrylate-silicone lens reported on. Therefore, the comments argue that the articles cannot constitute adequate valid scientific evidence of the safety and effectiveness of all contact lenses made of polyacrylate-silicone and proposed for reclassification. The comments state that Ref. 30 defines success as the ability to wear the lens for 10 hours per day, but includes no data from which to determine either safety or effectiveness, i.e., there are no data on epithelial staining, neovascularization, corneal edema, change in keratometry readings, corneal thickness, endothelial cell counts, or visual acuity before or after lens wear. Further, the comments state that although Ref. 31 includes most of the data believed to be necessary to evaluate a lens, it reports on only 46 patients and does not indicate how long the patients in the study were followed.

FDA agrees with these comments. All the data referred to by the comments are essential to any determination of the safety and effectiveness of a contact lens. Ref. 30 contains insufficient data to allow a scientific judgment of the safety and effectiveness of the lens under study. Ref. 31, with only 31 successful study patients and an indefinite followup period, is insufficient to demonstrate the safety and effectiveness of the lens under study because the study population is too small to generalize in a meaningful way and because no quantitative data are provided for any significant evaluation criterion except edema. It necessarily follows that because the data included in Refs. 30 and 31 do not provide sufficient valid scientific evidence of the safety and effectiveness of the lenses studied by the investigators, Refs. 30 and 31 cannot establish the safety and effectiveness of lenses not included in the studies.

12. A few comments, including a comment from the lens' manufacturer, discuss Refs. 30 and 31 of the proposal and state that the material used to make the lenses in these studies, identified only as POLYCON®, has been replaced by an improved material, POLYCON II® and tinted POLYCON II®. The comment from the manufacturer points out that the two latter lenses were approved by FDA only after preclinical and clinical studies following FDA's contact lens guideline demonstrated that lenses made of the new materials were safe and effective. The comment from the manufacturer further states that POLYCON® and POLYCON II® materials differ in polymer constituent ratios with concomitant differences in oxygen permeability and wettability, major factors in determining safety and effectiveness. The comments argue that FDA never would have approved the PMA for the POLYCON® lens, much less the POLYCON II® lens, on the basis of the data in the cited references. Consequently, the data cannot be an adequate basis for reclassification of the general category of polyacrylate-silicone lenses.

FDA agrees with these comments. FDA required complete nonclinical laboratory studies and clinical investigations for the POLYCON II® and tinted POLYCON II® lenses because changes had been made in the polymer ratios in the first case, and in certain polymer constituents in the second case. The evidence of safety and effectiveness of lenses of POLYCON® was therefore determined to be inapplicable to POLYCON II® and to tinted POLYCON II®. The data in the cited studies would not have been adequate to support premarket approval of POLYCON® and would have been considered inapplicable to POLYCON II®. It follows that the data in the cited studies are insufficient to show the safety and effectiveness of polyacrylate-silicone lenses as a generic type of device for the purpose of reclassification.

13. Six comments submitted data from clinical investigations of two different polyacrylate-silicone contact lenses, the Paraperm O_2™ and the Optacryl 60, covering a total of approximately 1,100 patients. One of the comments also included data from the laboratory testing (preclinical evaluation) of the Optacryl 60 lens. The comments argue that these data, most of which were the same as the clinical and preclinical data submitted in PMA's for these lenses, constitute ample valid scientific evidence of safety and effectiveness to serve as the basis for reclassification of rigid gas permeable lenses made of polyacrylate-silicone. The comments further argue that similarity of favorable results between the different varieties of polyacrylate-silicone show that the polyacrylate-silicone lenses constitute a generic type of device and that changes in polymer ratios do not give rise to divergent clinical results.

FDA disagrees with these comments. Questions concerning the completeness of the submitted data are discussed in paragraph 14 of this document. Those questions aside, none of the comments contains polymer formulation or manufacturing processes or any other information that

would allow characterization of the lenses studied, and as explained in sections II.B. and C. and paragraphs 23 and 24 of this document, evidence of the safety and effectiveness of a specific polyacrylate-silicone lens cannot be generalized to another polyacrylate-silicone lens without such information.

Taken at face value the data submitted with these comments support the conclusion that the lenses designated as the Paraperm O_2™ and Optacryl 60 are safe and effective. However, because the polymer ratios of the two lenses were not identified in the comments, conclusions pertaining to the effect on safety and effectiveness of differences in polymer ratios cannot be drawn. The assumption that the polymer ratios of Paraperm O_2™ and Optacryl 60 are different only allows the conclusion that polyacrylate-silicone lenses of more than one polymer ratio may be found to be safe and effective. It does not logically follow that changes in polymer ratios do not give rise to divergent clinical results.

Changes in the ratio of the principal ingredients of polyacrylate-silicone polymers, as illustrated by the following table, adapted from a table in a U.S. Patent for a polyacrylate-silicone lens material (Ref. 1), can be expected to result in significant changes in the oxygen permeability of lenses made from the ingredients listed in the table. Differences in oxygen permeability of the magnitude shown on the chart can be expected to give rise to divergent clinical results that significantly affect safety and effectiveness (Refs. 1 and 2).

Composition				
SIGMA	*EGMA*	*EDMA*	*MMA*	*Oxygen permeability* (Dk)
	parts			*mL.cm./cm.²sec.cm.Hg*
30	5	5	60	3.0×10^{-10}
40	7	5	48	6.2×10^{-10}
50	9	5	36	11.4×10^{-10}
60	11	5	24	18.4×10^{-10}
70	13	5	12	25.5×10^{-10}
80	10	5	5	31.8×10^{-10}

NOTE:

EGMA: Ethylene glycol monomethacrylate

EDMA: Ethylene glycol dimethacrylate

MMA: Methyl methacrylate

SIGMA is identified in the text of the patent as: Methyldi-(trimethylsiloxy)sylylpropylglycerol methacrylate.

Oxygen permeability (Dk) is expressed as the product of the diffusion coefficient for O_2 movement in the material (D) and the solubility constant for O_2 in the material (k).

14. Two comments question whether the safety and effectiveness data submitted with other comments on the Paraperm O_2™ and Optacryl 60 contact lenses constitute valid scientific evidence of the safety and effectiveness of these lenses. The comments point out that the data submitted cover approximately 1,100 subjects whereas the studies included more than 100,000 subjects. The comments question the basis for selection of the subjects included in the submitted data, whether the selection process biased the re-

sults of the studies, what the incidence was of adverse reaction in the total study population, and what efforts FDA has made to establish that these data do not represent a select subject population or group. The comments argue that if these questions are open, the data cannot be considered to be valid scientific evidence of safety and effectiveness.

In general, absent information about effectiveness and the incidence of adverse reactions in a total study population, and how the data submitted were selected from those available, FDA cannot determine whether the submitted data show, by valid scientific evidence, that an investigational device is safe and effective (see, e.g., § 860.7(f)(1)(ii) and (v)). In any event, because the lenses in the clinical investigations are only identified by general family of material, i.e., polyacrylate-silicone, brand name, and manufacturer, and no information is provided to characterize them by polymer formulation or manufacturing processes, the data do not and cannot show the safety and effectiveness of polyacrylate-silicone lenses as a generic type of device for the purpose of reclassification (see sections II.B. and C. and paragraphs 13, 23, and 24 of this document).

15. Two comments state that the data from the clinical investigations of the Paraperm O_2™ and the data from nonclinical laboratory studies and clinical investigations of the Optacryl 60 polyacrylate-silicone rigid gas permeable lenses, discussed in paragraphs 13 and 14 of this document, have been reviewed by the Ophthalmic Device Section of the Ophthalmic; Ear, Nose, and Throat; and Dental Devices Panel (the Section), an FDA advisory committee, during the Section's review of PMA's for the subject lenses. The comments argue that because the Section recommended approval of the PMA's for the Paraperm O_2™ lens and the Optacryl 60 lens, the data constitute valid scientific evidence within the meaning of § 860.7(c).

The question whether the data constitute valid scientific evidence of the safety and effectiveness of the studied lenses is discussed in paragraph 14 of this document. FDA advises that during the Section's review of the PMA's, the Section did not consider all the issues relevant to reclassification, e.g., the adequacy of the characterization of the devices or the adequacy of class I or class II to provide reasonable assurance of the safety and effectiveness of the devices. In any event, a PMA approval recommendation from an advisory committee simply is a recommendation and is not a determination by FDA that data in the PMA constitute valid scientific evidence.

16. More than 100 comments were received from professionals in the contact lens industry who regularly prescribe, fill prescriptions for, and fit contact lenses. More than 80 of these comments were from persons who identified themselves as investigators of polyacrylate-silicone contact lenses. As defined in § 812.3(i) of the regulations providing procedures for the conduct of clinical investigations of devices (the IDE regulations) (21 CFR 812.3 (i)), an investigator is an individual who gathers safety and effectiveness data for a sponsor who intends to seek premarket approval for a device. Each of the more than 100 comments favors reclassification of polyacrylate-silicone lenses from class III into class I.

FDA responds to these comments in paragraphs 17 to 21 of this document.

17. The comments from investigators argue that the data gathered as a result of the investigators' studies and similar investigations provide more than ample valid scientific evidence of the safety and effectiveness of polyacrylate-silicone contact lenses. Some investigators, including one investigator who studied 1,100 polyacrylate-silicone lenses, one who studied 3,000 polyacrylate-silicone lenses, and one who studied 7,000 polyacrylate-silicone lenses, cite the number of lenses studied.

FDA disagrees with these comments, the number of lenses investigated notwithstanding. FDA is prohibited by section 520(c) of the act from using as the basis for the reclassification of a device trade secret or confidential commercial information obtained under section 520(g) of the act (exemption for devices for investigational use). Consequently, except for those trade secret and confidential commercial data from clinical investigations that were made public in other comments and that are discussed elsewhere in this document, such data gathered by investigators are not available to FDA for the purpose of reclassification.

18. As evidence of safety, more than 30 investigators state that in their use of polyacrylate-silicone contact lenses, they have observed no adverse reactions.

Statements by individual investigators that no adverse reactions were found do not constitute valid scientific evidence within the meaning of § 860.7 of the regulations. Section 860.7(c)(2) states in part " • • • reports lacking sufficient details to permit scientific evaluation • • • are not regarded as valid scientific evidence to show safety or effectiveness." To meet the test of valid scientific evidence and permit scientific evaluation such reports need to include, at a minimum, a uniform scientifically acceptable definition of adverse reaction, the number of patients studied, and comprehensive summaries of the results of examinations for edema and staining as well as slit lamp examinations, and of all reports of discomfort, blurred vision, and of patients who discontinued use of the lenses or were otherwise lost to followup.

19. Several comments from investigators argue that when all other things are equal, the polyacrylate-silicone lenses that have been subjected to clinical investigations are superior to PMMA lenses because the former have been shown to be gas permeable and, thus, provide better oxygenization of the cornea. These comments state that this increase in oxygenization results in reduced edema

and greater wearer comfort, and allows the lens to be tolerated by the wearer for a longer period of time than PMMA lenses. There are no significant differences in the machining (lathing, grinding, and polishing) characteristics of the two materials, according to the comments. Therefore, the comments argue that any lens that can be made of PMMA also can be made of polyacrylate-silicone. Consequently, polyacrylate-silicone lenses should not be classified into a higher class than lenses made of PMMA, which FDA has proposed to classify into class II.

FDA disagrees with these comments. The classification of contact lenses made of PMMA is not legally relevant to the classification of rigid gas permeable lenses. As discussed in the September 30, 1975 notice (40 FR 44845), contact lenses made of PMMA have been marketed in the United States since the early 1950's. Due to their extensive history of safe and effective human use, PMMA lenses were regulated as devices prior to the enactment of the amendments and thus never required administrative approval for marketing. In contrast, rigid gas permeable lenses were first marketed in the United States in the late 1970's and always have required premarket approval. Indeed, since the introduction of hydrophilic (soft) contact lenses in the 1960's, FDA has regarded all contact lenses other than those made of PMMA as new drugs requiring premarketing clearance (see paragraph 1 of this document). The September 30, 1975 notice explains that the agency's decision to require such clearance for all contact lenses made from non-PMMA materials " • • • was based on a recognition that new plastic materials that had not been shown to be safe and effective [for use] were being introduced for use in the manufacture of contact lenses. The introduction of these new materials led to new lens design and use, new manufacturing methods, and new methods for lens care. [FDA] is concerned that the use of these contact lenses may result in serious eye damage if the new material of which they are composed is unsafe for

use in the eye, if the user cannot feasibly care for the lenses, or if the highly complex procedures for the manufacture of these lenses are not carefully controlled to assure a product of uniform quality" (40 FR 44845).

As explained in paragraph 1 of this document, rigid gas permeable lenses were automatically classified into class III on the enactment date of the amendments in accordance with section 520(l)(1)(B), (C), and (E) of the act. Such lenses may only be reclassified into class I or class II in accordance with the provisions of the act and the regulations as discussed in the preamble to the proposed rule (47 FR 53404) and in section II.A. of this document.

Neither the safety nor the effectiveness of polyacrylate-silicone lenses has been established by valid scientific evidence other than in PMA's. Furthermore, FDA is not aware of, and no comments provided, evidence that there are no significant differences in the machining characteristics of PMMA and any of the formulations of polyacrylate-silicone used to manufacture any of the investigational lenses about which comments were submitted. On the contrary, one comment from an investigator cites machining differences, including increased tool wear, longer polishing times, and reduced yield for polyacrylate-silicone compared to PMMA. FDA believes that these differences reflect potential significant differences in the characteristics of PMMA and polyacrylate-silicone lenses, for example, surface finish and uniformity.

20. Ten comments from investigators note that approved lenses are routinely modified in optical laboratories to improve the fit for specific patients. The potential superior fit of custom fitted lenses is cited as an advantage of the investigational lenses over approved lenses, and as an argument for reclassification. Custom fitted lenses, specifically the polyacrylate-silicone lenses under investigation by those submitting comments, result, according to the comments, in a better fit and concomitant better comfort

and tolerance for those patients whose eyes do not precisely match the dimensions of approved lenses. Approved polyacrylate-silicone lenses are only available in a limited number of configurations, according to the comments. Therefore, the comments argue that custom fitted investigational polyacrylate-slicone lenses allow successful fitting of a larger portion of the potential lens wearing population than is currently possible with approved polyacrylate-silicone lenses. Custom fitted lenses also are said to allow a more perfect fit for those patients for whom the best fit of an approved lens is a compromise.

FDA acknowledges that some portion of the user population cannot always be fitted successfully from a fixed set of lenses, and that some of these individuals might be fitted successfully through modification of off-the-shelf lenses. FDA notes that nothing in the act or the regulations forbids optical laboratories from modifying approved lenses to meet the needs of specific patients so long as the specifications of the lenses, as modified, remain within the specifications of the PMA's for the approved lenses. For this reason, there is no basis for the argument that investigational lenses are subject to "custom fitting," while approved lenses are not. Further, the comments appear to presuppose that the investigational lenses in question have been shown to be safe and effective in the first place; the comments do not add to the body of valid scientific evidence that is required to estabilsh the safety and effectiveness of the lenses proposed for reclassification. The comments, therefore, are not relevant to the question of reclassification.

21. More than 20 comments from investigators argue that FDA should not regulate prescribing and fitting of polyacrylate-silicone lenses by limiting reclassification to spherical lens designs. According to these comments, prescribing and fitting are best left to the experts in the practice of optometry and ophthalmology. These comments

further argue that competition among laboratories that make lens blanks into finished lenses and between fitters or prescribers of lenses will rapidly force off the market those members of each group who provide lenses that are either uncomfortable or do not provide adequate visual acuity. These comments also point out that FDA approval of a contact lens does not prevent poor fitting or prescribing and claim that because the choice of designs in off-the-shelf lenses is limited, the problem of poor fitting or prescribing is exacerbated.

FDA limited the proposed rule to reclassify rigid gas permeable lenses to spherical designs because of a complete lack of valid scientific evidence of safety and effectiveness of lenses of other than spherical designs. No such evidence of the safety and effectiveness of lenses of other than spherical designs was submitted during the comment periods or at the public hearing on the proposal (see paragraph 22 of this document). FDA recognizes that its approval of a PMA for a contact lens will not prevent practitioners from erring when fitting or prescribing the lens; however, the inability of the agency to prevent such errors in no way justifies the reclassification of a lens into class I or class II.

22. Several comments state that nonspherical lenses, including toric, bitoric, and bifocal lenses, should have been included in the proposed reclassification of rigid gas permeable lenses. The comments argue that any gas permeable lens material that is suitable for spherical contact lenses will be equally suitable for nonspherical lens designs. The historical use of PMMA for lenses of both spherical and nonspherical designs and the similarities of rigid gas permeable materials to PMMA are cited in support of this argument. Other comments argue that nonspherical rigid gas permeable lenses were correctly excluded from the proposed rule because there is insufficient valid scientific evidence of the safety and effectiveness of such lenses for any indication.

Because FDA is withdrawing the proposed reclassification of rigid gas permeable lenses, the question whether nonspherical lens designs should have been included in the proposal is moot. FDA advises, however, that spherical, toric, bitoric, and bifocal lenses are indicated for different ametropias and that there is no valid scientific evidence, other than in PMA's, that any nonspherical rigid gas permeable lens is safe and effective for any indication. FDA recognizes that many characteristics of contact lenses that affect safety are material-specific and that these characteristics, e.g., toxicity and oxygen permeability, will not be altered by changes from spherical to nonspherical lens design. Other characteristics affecting effectiveness, as well as safety, are functions of design and material in combination. Thus, for example, valid scientific evidence that spherical and toric lenses made of the same material are safe and effective for the correction of hyperopia, myopia, and astigmatism do not constitute such evidence that a bifocal lens that (1) is also made of that material and (2) combines design elements of the spherical and toric lenses is effective or safe for the correction of presbyopia (see *United States* v. *Wesley-Jessen, Inc.*, Civil No. 82C874 (N.D. Ill., March 11, 1982) (transcript of proceedings)).

The machining and polishing characteristics and hence the lens surface characteristics of rigid gas permeable materials are not identical to those of PMMA, nor are wetting characteristics, rigidity, or balance. Such differences may or may not result in differences in edema, staining, centration, orientation, and tear pumping characteristics. Therefore, the safety and effectiveness of PMMA lenses of spherical and nonspherical designs do not establish, by valid scientific evidence, the safety and effectiveness of rigid gas permeable lenses of spherical or nonspherical designs.

D. Adequacy of Characterization

23. One comment argues that characterization of rigid gas permeable lenses by materials is adequate for the

purpose of reclassification, citing the proposed rule to classify PMMA contact lenses (47 FR 3746), and quoting the preamble to the proposed rule to classify ophthalmic devices (47 FR 3695): "The identification statement is necessarily broad because it applies to a category or type of device rather than to a specific device. * * * It is not practical for FDA to publish an identification of each type of device that is so detailed as to anticipate every product feature that may be relevant in determining whether a new device is substantially equivalent to previous devices classified by the regulation."

As a general rule, characterization of a device by material, at least in part, for the purpose of identifying the generic type of device in a classification regulation is appropriate. In the case of rigid gas permeable lenses, however, FDA has concluded that such characterization is not feasible (see sections II.B. and C. and paragraphs 13 and 24 of this document).

24. Several comments state that a lens defined as consisting of a material described as polyacrylate-silicone can include a broad range of characteristics and that this is not a substantive definition. The comments note that patents based upon new composition of materials for the manufacture of rigid gas permeable lenses reveal large numbers of materials falling within the broad scope of polyacrylate-silicone. The comments claim that these materials are unique beyond all prior art, prior art including the polyacrylate-silicone material of the POLYCON® lens evaluated in Refs. 30 and 31 of the proposal (also see paragraphs 11 and 12 of this document). The comments argue that it is neither reasonable nor scientifically valid to extrapolate evidence of safety and effectiveness from lenses of this one material, or any unique materials for which data may be available, to lenses of other unique materials within the general type of material, but for which data are not available. The comments cite several references, in-

cluding patents, that illustrate some of the changes in characteristics that result from changes in formulation or process. The comments conclude that whether a contact lens made from a particular polyacrylate-silicone material is safe and effective can be determined only by conducting preclinical and clinical evaluations of the type identified in FDA's contact lens guideline. Consequently, the comments state, evidence of the safety and effectiveness of a specific lens of a particular polymer formulation and manufacturing process can only serve as evidence of the safety and effectiveness of that lens. Such evidence fails to demonstrate the safety and effectiveness of a generic type of device.

FDA agrees with the comments. The term silicone acrylate, even when limited by the definition in the preamble to the proposed rule (47 FR 53406): "Polyacrylate-silicone copolymer contact lenses consist of complex siloxanyl methacrylate polymers * * *. Such lenses contain PMMA for rigidity and polymerized silicone for oxygen permeability", or by the definition offered by the comments discussed in paragraph 26 of this document, encompasses a virtually infinite set of combinations of principal and adjunctive ingredients. The number of such combinations suitable for the manufacture of contact lenses, albeit perhaps finite, is unknown, as is the range of variation of ingredient ratios, polymerization processes, and resultant material characteristics. (Much of this information may be known to manufacturers of contact lenses, but none of it was included in or submitted with any of the comments, and FDA is prohibited by sections 301(j) and 520(c) of the act from disclosing such information from PMA's or files for investigational devices under development pursuant to IDE's because such information constitutes trade secret data.)

As discussed in sections II.B. and C. and paragraphs 13 and 23 of this document, the existence of a predictable relationship between a lens polymer formulation, manu-

facturing process, physical and other quantifiable parameters, and its safety and effectiveness has not been demonstrated by any valid scientific evidence. Lacking knowledge of such a relationship one cannot infer from evidence that any rigid gas permeable lens of unique polymer formulation, produced by a unique process, and having unique properties is safe and effective, that any other rigid gas permeable lens also is safe and effective unless both lenses are sufficiently characterized to demonstrate that they are virtually identical.

Any effort to use the evidence of safety and effectiveness of a specific rigid gas permeable lens or lenses as the basis for reclassification of a generic type of lens, regardless of how narrowly or broadly that generic type of lens is identified, requires detailed characterization of the lens or lenses from which the evidence is drawn and the lenses to which the characterization applies. This characterization necessarily includes details of raw materials, polymer constituents and ratios, and manufacturing information. Without such characterization there is no basis for extrapolation of evidence of the safety and effectiveness from one lens to any other.

E. Adequacy of General Controls

Several comments argue for and several comments argue against the adequacy of class I to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses. These arguments center around the adequacy of two principal provisions of the general controls, premarket notification under section 510(k) of the act and current good manufacturing practice requirements under section 520(f) of the act and the current good manufacturing practice (CGMP) regulations (21 CFR Part 820).

25. One comment argues that the premarket approval process does not ensure safe and effective contact lenses or their accessories. The comment cites examples of how the

marketplace allegedly has exposed flaws in or led to improvements of lenses and lens accessories that had received FDA approval, and concludes that introduction of new daily-wear contact lenses by the premarket notification process would be as safe as, and more efficient than, introduction of such lenses under the premarket approval process. The comment argues, therefore, that the lenses should be reclassified into class I.

FDA disagrees with this comment. The legal standard governing reclassification under section 513(e) of the act is discussed in the preamble to the proposed rule (47 FR 53404) and in section II.A. of this document. FDA recognizes that approval of a PMA for a contact lens or a contact lens accessory does not always ensure that the device will perform flawlessly in the marketplace. In addition, approval of a PMA does not protect or prevent a device from being rapidly replaced by a new or improved device as a result of needs expressed by consumers and practitioners. This is especially true in the contact lens industry, where the state-of-the-art is one of rapid and continued innovation and refinement. Nonetheless, opinions about the adequacy of premarket approval to ensure safe and effective contact lenses cannot justify reclassification and do not add to the body of valid scientific evidence that is required to establish the safety and effectiveness of the lenses proposed for reclassification.

26. Two comments provide a proposed definition of polyacrylate-silicone lens materials and a set of parameters with assigned acceptance limits. The proposed definition of polyacrylate-silicone reads: "copolymers composed principally of simple alkyl acrylate or alkyl methacrylate monomers and silicone substituted acrylate or methacrylate monomers. Additional components present in minor proportions include the crosslinkers, wetting agents, stabilizers, and catalysts currently used to manufacture crosslinked PMMA. The silicone-substituted acrylate or meth-

acrylate monomer is further identified as an acryloxy or methacryloxy alkyl or aryl substituted silicone. A silicone is further defined as a polymeric chemical structure having a backbone of alternating silicon and oxygen atoms." The set of parameters includes composition, luminous transmittance, index of refraction, oxygen permeability, dimensional stability, tensile strength, flexural strength, cytotoxicity, eye irritation, resistance to bacteria, extractables, preservative uptake, wettability, and care system compatibility. The comments argue that polyacrylate-silicone lenses whose material met the definition and all the parameters, including certain preclinical testing requirements, would be safe and effective, and that the set of parameters would therefore be adequate to determine whether any new lens was substantially equivalent to a reclassified lens. The comments further argue that evidence of safety and effectiveness need not include data and information on lens polymer formulation or manufacturing process to provide an adequate basis for reclassification because evaluation against the parameters would screen out all unsafe and ineffective lenses.

FDA disagrees with these comments. The definition provided in the comments describes a broad group of polymers that could be accurately titled, "polyacrylate-silicone." As pointed out in one of the two comments, however, materials meeting the definition suggested by the comments could include any number of formulations that were either suitable or unsuitable for the manufacture of safe and effective contact lenses. The definition contains no provisions to distingiush between suitable and unsuitable polyacrylate-silicone materials, much less between safe and effective and unsafe and ineffective lenses made from the materials.

Use of a set of parameters with assigned acceptance limits without valid scientific evidence that lenses meeting such limits would be safe and effective provides no assurance of lens safety and effectiveness and is inadequate to

serve as a basis for determining substantial equivalence. As stated in section II.E. and paragraph 34 of this document, FDA is unaware of any combination of nonclinical laboratory studies capable of predicting with reasonable assurance the safety and effectiveness of any contact lens on the human eye. In addition, neither comment contained, and FDA is unaware of, any valid scientific evidence that a lens meeting the parameters included in the comments, or any other set of criteria, would be safe or effective, or that use of the parameters included in the comments, or any other set of criteria, would provide an adequate basis on which to determine whether a new lens was substantially equivalent to a reclassified lens in terms of safety and effectiveness. Neither the parameters included in the comments nor any other set of criteria could serve as a basis for reclassification unless they were supported by valid scientific evidence showing that their use in determination of substantial equivalence would provide reasonable assurance of the safety and effectiveness of the new lens as compared to the reclassified lens. As discussed in sections II.B. and C. and paragraphs 13, 23, and 24 of this document, lacking such evidence, information characterizing lenses by polymer formulation and manufacturing processes is essential to any evidence of safety and effectiveness that could serve as a basis for reclassification, and would be essential to determine substantial equivalence of any new lens in the event that any rigid gas permeable lens were reclassified.

27. Several comments object to the statement in the preamble to the proposal concerning the information that FDA would require to be included in a premarket notification submission under section 510(k) of the act for a contact lens. The comments argue that requiring all this information would exceed FDA's authority under section 510(k) of the act and would amount to a "mini-premarket approval" requirement.

FDA agrees in part with these comments. In the preamble to the proposal, FDA stated that the manufacturer of a contact lens should be prepared to demonstrate substantial equivalence in terms including but not limited to, design; composition; optical transmission and homogeneity, and index of refraction; and other physical properties including oxygen permeability, chemical and physical stability, tensile and flexural strength; biocompatibility, including cytoxicity, eye irritation and nonsupport of bacterial growth; impurities; leachables; heavy metal levels; preservative uptake and release; and lens care/cleaning regimen compatibility as well as compliance with the CGMP regulations. All this information concerns the basic characteristics of contact lenses. If FDA had reclassified the lenses, such information would have been needed by FDA in a premarket notification submission to determine whether a new contact lens was substantially equivalent to a reclassified lens in terms of safety and effectiveness.

Section 807.87(h) of the regulations governing premarket notification procedures provides that FDA may require the submission of any information that is necessary for FDA to determine whether a device is substantially equivalent in terms of safety and effectiveness to a preamendments device or to a transitional or postamendments device reclassified into class I or class II. For a contact lens, this information may include any or all of the information cited above, and may also include, where necessary to determine comparability of safety and effectiveness, limited data from nonclinical laboratory studies and clinical investigations.

As discussed in sections II.C. and E. and paragraphs 13 and 34 of this document, extensive data from studies and investigations are necessary to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses. FDA recognizes that requiring such much information would result in the submission of data so complete

as to be indistinguishable from the data needed to determine the safety and effectiveness of a device in the first instance rather than on a comparison basis. The data required in a premarket notification submission would then be indistinguishable from the data required in a PMA. FDA agrees that imposing such a requirement as an *a priori* condition for determining substantial equivalence would exceed the authority of section 510(k) of the act and Subpart E of Part 807. If such extensive submissions would be necessary to determine substantial equivalence in terms of safety and effectiveness of the device, it follows that class I controls would be inadequate to provide reasonable assurance of safety and effectiveness of the device.

28. One comment argues that if the testing of lenses that is necessary to show that a lens is substantially equivalent to a reclassified lens approximates that which would be necessary for a premarket approval application, "such expansion of the 510(k) concept would not be justified."

FDA agrees with the comment. Where, as in this case, the type and amount of information that would be required to show substantial equivalence in terms of safety and effectiveness would approximate the type and amount of information required to obtain approval of a PMA for a device, reclassification of the device based on reliance on the process under section 510(k) of the act would not be justified.

29. One comment argues that if FDA requires lenses of new materials to be virtually identical to lenses of reclassified materials, it will be impossible to market alternate contact lens materials under section 510(k) of the act. The comment claims that such an interpretation of the substantial equivalence requirement would hinder the marketing of improved rigid gas permeable materials.

FDA agrees that if it had reclassified any of the lenses proposed for reclassification and required that any new

lens be virtually identical to a reclassified lens, it would not have been possible to market under section 510(k) of the act lenses made of alternate materials. Whether such a requirement would have hindered the marketing of "improved" rigid gas permeable lenses is unknown. FDA advises, however, that any postamendments device, including any contact lens, that is not substantially equivalent to a preamendments device or a postamendments device that has been reclassified is automatically classified into class III under section 513(f) of the act and cannot legally be marketed unless it is the subject of an approved PMA or has been reclassified.

30. One comment states that all CAB and polyacrylate-silicone materials that are "equally suitable for their intended use, as compared to already approved lens materials, should be recognized as substantially equivalent to those materials * * *".

FDA disagrees with the comment. The act applies to devices as defined in section 201(h) of the act (21 U.S.C. 321(h)), rather than raw materials. If, however, the act applied to raw materials, any postamendments raw material, including any contact lens raw material, that was not substantially equivalent to a preamendments raw material or a postamendments raw material that had been reclassified would be automatically classified into class III under section 513(f) of the act and could not legally be marketed unless it were the subject of an approved PMA or had been reclassified. FDA notes that the comment provides no definition of the concept of "equal suitability."

31. Several comments state that enforcement of the CGMP regulations is essential to ensure adequate quality control of contact lens manufacture and to prevent the distribution of unsafe or ineffective lenses. Some of these comments point out that according to the preamble to the proposed rule (47 FR 53405), manufacturers would be required to demonstrate compliance with the CGMP regu-

lations to establish substantial equivalence. Some of these comments argue that to ensure such compliance, FDA would have to inspect the manufacturing sites identified in premarket notification submissions and that such inspections could not be scheduled and completed in the 90 days allowed for review by FDA of such submissions. In such case, the comments note, the person submitting the premarket notification could market lenses without an inspection by FDA of the person's manufacturing facility. Some of these comments also note that FDA has no requirements for mandatory CGMP inspections of facilities in which class I devices are manufactured and that the lack of such regular inspections could result in the marketing of unsafe or ineffective contact lenses, if the lenses were reclassified into class I.

FDA agrees that compliance with the CGMP regulations is essential to ensure the manufacture of safe and effective contact lenses because of the need for consistency in formulating, processing, and finishing these devices. Because FDA is withdrawing the proposed rule, the question whether FDA may require the inclusion in a premarket notification submission of sufficient information to determine whether a manufacturer's facility is in compliance with the CGMP regulations as part of the premarket notification review is moot. FDA, of course, has the authority to conduct CGMP inspections of any device establishment, including any device manufacturing facility, regardless of the classification of a device, to determine whether the facility is in compliance with the regulations.

F. Adequacy of Class II

32. Several comments, including those that responded explicitly to questions 1.d. and e. of the preamble to the proposed rule, argue that class II would be the most appropriate regulatory class for rigid gas permeable lenses. Most of these comments also argue that any reclassification

of rigid gas permeable lenses into class II should not take effect before a perfo[illegible]nce standard under section 514 of the act is establish[illegible]nch lenses. Some comments argue that there is, while others argue that there is not, sufficient valid scientific evidence to establish such a standard. A number of comments state that a performance standard covering lens properties or design characteristics, such as the clinically significant properties and design characteristics cited in the preamble to the proposed rule (47 FR 53405), would be sufficient to provide reasonable assurance of safety and effectiveness of the lenses. Several other comments argue that any such standard needs to include a requirement for clinical investigation of the lenses.

FDA stated in the preamble to the proposed rule (47 FR 53405):

> This proposal to reclassify daily wear spherical contact lenses composed of CAB or polyacrylate-silicone into class I, rather than into class II upon the effective date of a performance standard promulgated in accordance with section 514 of the act, is based on FDA's tentative conclusion that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of such lenses. FDA believes that sufficient information exists to establish a section 514 standard to provide reasonable assurance of the safety and effectiveness of the device; however, FDA does not believe it is necessary to establish such a standard to provide such assurance.

FDA has determined that its tentative conclusion about the adequacy of general controls was in error and that sufficient information does not exist to establish a performance standard under section 514 of the act. The requirement that reclassification of a device be based on valid scientific evidence of safety and effectiveness applies to reclassification from class III into class II, as well as to reclassifica-

tion from class III into class I. As discussed in sections II.B. and II.C. of this document, FDA has concluded that there is insufficient valid scientific evidence other than in PMA's to show that rigid gas permeable lenses are safe and effective. For this reason, FDA cannot conclude that such lenses should not remain in class III, or determine whether reclassification into class II, as opposed to class I, would provide reasonable assurance of their safety and effectiveness. Furthermore, any performance standard that addressed and set parametric limits on lens properties or design characteristics, such as the clinically significant properties and design characteristics cited in the preamble to the proposed rule, the set of parameters listed and discussed in section II.D. and paragraph 26 of this document, or the material properties delineated in ANSI Z80.6-1983 (see paragraph 33 of this document) would have to be based on valid scientific evidence that the standard would provide reasonable assurance of the safety and effectiveness of the lenses covered by the standard. As discussed in section II.D. and paragraphs 26 and 32 of this document, FDA has concluded that no such evidence is publicly available. Absent sufficient information to establish a performance standard to provide reasonable assurance of the safety and effectiveness of a device, the device may not be reclassified into class II, because under section 513(a)(1)(B) of the act, a class II device is a device for which, among other things, "there is sufficient information to establish a performance standard to provide" reasonable assurance of safety and effectiveness.

FDA believes that in lieu of a standard under section 514 of the act prescribing performance criteria, a standard under that section prescribing testing and evaluation criteria to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses might be feasible. At this time, however, such a standard could not be developed based on information available in the public domain. FDA notes that if there were sufficient valid scien-

tific evidence to develop a testing and evaluation standard, its existence would serve as a principle part of the basis for the reclassification into class II of any rigid gas permeable lens to be covered by the standard. Consequently, any resulting reclassification could not become effective prior to the effective date of such standard.

33. A few comments suggest that a voluntary standard (ANSI Z80.6-1983) titled, "American National Standard for Ophthalmics—Conventional Hard Plastic Contact Lenses—Physiochemical Properties," published by the American National Standards Institute, Inc. (ANSI) could serve as the basis for the establishment of a performance standard under section 514 of the act in the event that FDA decided to reclassify rigid gas permeable lenses into class II rather than class I. Some of these comments argue that the existence of ANSI Z80.6-1983 is adequate evidence that there is sufficient information to develop a performance standard. One comment submitted a copy of ANSI Z80.6-1983 to the record.

No comments submitted, and FDA is unaware of, any evidence that a lens made of a material that meets ANSI Z80.6-1983 is safe and effective. While it may be feasible to show, through a series of measurements of approved rigid gas permeable lenses, that all such lenses meet the subject standard, there is no basis to conclude that any other lens that meets the standard would necessarily be either safe or effective. Quite the contrary, ANSI Z80.6-1983 addresses only a limited number of physiochemical properties of contact lens materials. Adherence to the voluntary standard would not ensure that lenses made from materials meeting the standard would be nontoxic, biocompatible, or effective.

G. Need for Clinical Trials

34. Several comments state that clinical trials are necessary to provide reasonable assurance of the safety and

effectiveness of rigid gas permeable lenses. Some of the comments state that if such lenses were reclassified, at least limited clinical trials would be necessary to establish the safety and effectiveness of lenses made of a new or modified material or lenses made by a new manufacturer. The comments argue that differences in lens polymer formulation, changes in manufacturing process or process control, or changes from one manufacturer to another can result in changes in lens' clinical performance that can only be adequately evaluated in a clinical trial. Two comments argue, on the contrary, that lenses meeting a definition of polyacrylate-silicone provided in the comments, and a set of parameters with assigned acceptance limits, also provided in the comments, would be safe and effective and therefore would not need clinical evaluation. Another comment states that the persons who claim that clinical trials are necessary to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses have failed to provide any valid scientific evidence that such trials are necessary.

Each of these comments and related arguments are summarized and addressed in sections II.C. and E. and paragraphs 13, 22, 24, and 26 of this document. FDA has regulated contact lenses as new drugs or class III devices for more than a decade, and is unaware of any combination of nonclinical laboratory studies capable of predicting the performance of any contact lens on the human eye. Nothing in the comments that provided the definition and the set of parameters, or in any other comments, establishes that clinical trials are not necessary to provide reasonable assurance of the safety and effectiveness of polyacrylate-silicone lenses, or that polyacrylate-silicone lenses whose material met the definition and the parameters would be safe and effective.

As stated in section II.E. of this document, FDA believes that the safety and effectiveness of a contact lens is a

function of the complex interrelationship of material, design, and manufacture that results in a unique set of physical, chemical, mechanical, and optical characteristics. When prescribed and fitted properly, a lens with this unique set of characteristics should provide safe and effective visual correction in a human eye with a specific diagnosed ametropia. FDA believes that contact lenses made from a new material, including material that has been significantly modified, contact lenses made to significantly modified designs, and contact lenses for which approval for a new indication is sought, cannot at this time be shown to be safe and effective without clinical, as well as preclinical, evaluation.

FDA agrees that none of the comments provided any valid scientific evidence that clinical trials are necessary to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses. As explained in paragraph 4 of this document, however, the burden of proof in this proceeding requires FDA (or the proponents of reclassification) to establish, by valid scientific evidence of safety and effectiveness, that rigid gas permeable lenses should not remain in class III and that class I (or class II) would provide reasonable assurance of the safety and effectiveness of such lenses. The opponents of reclassification are not required to provide any evidence to establish that reclassification is inappropriate.

H. Economic Impact of Reclassification

35. Many comments support reclassification from class III into class I on economic grounds.

FDA notes that only a few of the comments contain any economic data to support their claims, and that none of these data was substantiated by accompanying documentation. In any event, even if the claims were substantiated, FDA could not have legally reclassified any rigid gas permeable lens, nor could the agency legally reclassify any

other class III device into class I or class II, absent the requisite valid scientific evidence of safety and effectiveness (see the preamble to the proposed rule (47 FR 53404) and section II.A. of this document).

36. Many comments cite the current classification of rigid gas permeable lenses as "a completely unnecessary barrrier to competition" that threatens the viability and welfare of small businesses. The comments, citing recent poor business and layoffs, attribute the hardship of the small contact lens manufacturer to the current classification.

As explained in paragraph 1 of this document, all rigid gas permeable lenses are class III devices as a result of, among other things, (1) the September 30, 1975 notice and (2) section 520(l)(1)(E) and (l)(3)(D)(i) of the act. The 1975 notice was based on concerns about the safety and effectiveness of lenses consisting of polymers other than PMMA see paragraph 19 of this document). These concerns continue to justify classification of such lenses into class III, as discussed more fully in section II.B. and paragraphs 13, 23, 24, and 26 of this document. Thus. classification into class III is not "unnecessary." Furthermore, a number of small companies hold approved PMA's for non-PMMA lenses, including rigid gas permeable lenses. FDA notes that approved PMA's for several polyacrylate-silicone lenses cover a total of more than 250 contact lens finishing laboratories, and that the agency has advised each of the PMA holders how more such laboratories can be approved as additional manufacturing sites without the need for the PMA holders or the laboratories to gather additional clinical data. FDA has received no evidence of the cause of the poor business and resultant layoffs cited in the comments.

37. Several comments complain of the "de facto monopoly" held by large manufacturers that hold approved PMA's. One of these comments complained that the re-

quirements associated with securing premarket approval cost "in the neighborhood of $1 million."

FDA does not agree with the comments. Small companies can and do obtain approved PMA's. Although the figure of $1 million is unsubstantiated, FDA is aware that the requirements for premarket approval are stringent and as discussed in paragraph 36 of this document, has taken steps to make the premarket approval process less burdensome for the contact lens industry. The agency advises, however, that Congress chose to protect the data in PMA's from use by others seeking premarket approval and from use by others and by FDA for the purpose of reclassification (see the preamble to the proposed rule (47 FR 53404) and section II.A. of this document).

38. One comment claims that although the cost of rigid gas permeable lenses would decline as a result of reclassification, patients would have more fitting and other problems with the reclassified lenses, resulting in higher costs overall. The comment assumes that on average the patient wearing the reclassified lenses would require two additional professional office visits at $30 each for proper fitting. The comment further assumes 1,680,000 new patients, arriving at "an increase of $100,800,000 in avoidable health care costs."

FDA does not agree with this comment, which was not supported by any valid economic data. FDA therefore rejects this comment as speculative.

39. One comment argues that the economic benefits claimed by FDA for reclassification can be obtained without reclassification of rigid gas permeable lenses. The comment notes that since 1971 the number of manufacturers holding approved PMA's for hydrogel (soft) contact lenses, also a class III device, has increased from 1 to 30, with many small manufacturers obtaining approved PMA's. The comment also claims that the price of soft contact lenses has declined significantly over the years,

and predicts the same progression for rigid gas permeable lenses without reclassification.

FDA partially agrees with this comment. FDA has noted the increase in the number of approvals of PMA's for soft contact lenses, but FDA is unaware of any data to support the claims regarding costs or the assumption that rigid gas permeable lenses will follow the same progression.

40. One comment claims that the marginal economic benefits to late market entrants resulting from reclassification would be offset by increased risks to the consumer, and that reclassification would have an adverse impact on innovation.

FDA does not agree with this comment, which was not supported by any valid economic data. FDA therefore rejects this comment as speculative.

I. Contact Lens Accessories

41. One comment argues that rigid gas permeable lens accessories are not class III devices under section 520(l)(1)(E) of the act because such accessories are not devices which FDA, by a notice published in the FEDERAL REGISTER before enactment of the amendments, declared to be new drugs subject to section 505 of the act. Several comments argue that regardless of the classification or regulatory status of rigid gas permeable lenses, accessories for use with such lenses should be subject to the same level of regulatory control as the lenses because the accessories are an integral part of the safety and effectiveness of the lenses.

FDA advises that the term "device" includes "any • • • accessory" (section 201(h) of the act). Thus, accessories for use with rigid gas permeable lenses are class III devices under section 520(l)(1)(E) of the act because rigid gas permeable lenses are class III devices under that sec-

tion (see paragraph 1 of this document). Similarly, any accessory for use with a rigid gas permeable lens for which an NDA was pending on the enactment date, e.g., MESO Contact Lens, is a class III device under section 520(l)(1)(B) of the act, and any accessory for use with a rigid gas permeable lens for which an IND was in effect on the enactment date, e.g., MESO Contact Lens, CABCURVE® Contact Lens, POLYCON®, is a class III device under section 520(l)(1)(C) of the act. Furthermore, any rigid gas permeable lens accessory that is substantially equivalent to an accessory for use with a rigid gas permeable lens for which an NDA was pending or an IND was in effect on the enactment date is a class III device under section 520(l)(1)(D) of the act.

FDA also advises that any rigid gas permeable lens accessory for which an NDA was pending on the enactment date, e.g., BOILnSOAK®, PREFLEX®, is a class III device under section 520(l)(1)(B) of the act; that any rigid gas permeable lens accessory for which an IND was in effect on the enactment date, e.g., PREFLEX®, FLEX-SOL®, FLEX-CARE™, is a class III device under section 520(l)(1)(C) of the act; and that any rigid gas permeable lens accessory that is substantially equivalent to such an accessory covered by section 520(l)(1)(B) or (C) is a class III device under section 520(l)(1)(D) of the act.

FDA is withdrawing the proposed rule, and as discussed in paragraph 42 of this document, has concluded that there is insufficient valid scientific evidence of the safety and effectiveness of rigid gas permeable lens accessories to initiate proceedings to reclassify these devices. Accordingly, the question whether the lenses and the accessories should be subject to the same level of regulatory control regardless of the classification or the regulatory status of the lenses is moot.

42. Several comments argue that although there are no well-controlled clinical studies addressing the safety and

effectiveness of accessories used with rigid gas permeable lenses, reclassification of the accessories can be supported by the lack of significant reports of adverse effects associated with their use and by the substantial marketing experience associated with these devices. One comment states that accessory solutions for rigid gas permeable lenses should be reclassified because they have a substantial marketing history of safe and effective use with PMMA lenses. Comments opposed to the reclassification of rigid gas permeable lens accessories argue that clinical trials and class III controls are necessary to provide reasonable assurance of the safety and effectiveness of such accessories. These comments argue that there are numerous reports in the scientific literature of adverse reactions associated with contact lens accessories, such as bacterial infections, corneal ulcers, giant papillary conjunctivitis, eye irritation and discomfort, as well as allergic and sensitivity reactions. These comments also argue that contact lens solutions may cause temporary or permanent damage to lenses, e.g., changes in lens parameters, distortion, gummy deposits, or discoloration. These comments conclude that there is insufficient valid scientific evidence to demonstrate the safety and effectiveness of rigid gas permeable lens accessories, and, therefore, that FDA does not have a sufficient basis on which to reclassify such accessories.

The legal standard for reclassification set out in the preamble to the proposed rule (47 FR 53404), and reiterated in section II.A. of this document, applies to the issue of reclassification of rigid gas permeable lens accessories. To reclassify rigid gas permeable lens accessories, the act and the regulations require valid scientific evidence of safety and effectiveness to demonstrate why the accessories should not remain in class III and why class I or class II would provide reasonable assurance of their safety and effectiveness.

FDA recognizes that several accessories (e.g., disinfecting, cleaning, lubricating, and rewetting solutions) that

have been used with rigid gas permeable lenses also have been used with PMMA lenses. FDA believes, however, that the safety and effectiveness of accessories intended for use with rigid gas permeable lenses cannot be demonstrated solely on the basis of a history of substantial marketing experience with lenses made of significantly different materials and a lack of reports of adverse effects associated with the use of the accessories with lenses made of significantly different materials. In any event, DEN is not comprehensive; there currently are no reporting requirements applicable to PMMA lenses; and there is no history of substantial marketing experience of these accessories with rigid gas permeable lenses. FDA is unaware of, and did not receive in the comments, any valid scientific evidence of the safety and effectiveness of accessories intended for use with rigid gas permeable lenses. FDA, therefore, cannot determine whether class I or class II controls would provide reasonable assurance of the safety and effectiveness of rigid gas permeable lens accessories and may not at this time initiate proceedings to reclassify these devices.

J. Tinted Contact Lenses

43. One comment states that in amending section 706 of the act (21 U.S.C. 376), Congress could not have intended that devices already on the market, including tinted contact lenses, would be deemed to be adulterated on the date of enactment of the amendments.

FDA agrees in part, and disagrees in part, with the comment. FDA's responsibility for regulating color additives used in or on devices began on May 28, 1976, when the amendments became law. Among other things, the amendments expanded the coverage of the color additive provisions of the act, so that a color additive that is used in or on a device and that comes in direct contact with the body of man or other animals for a significant period of time is subject to regulation under section 706 of the

act. Section 706(a) provides that a color additive shall be deemed unsafe within the meaning of section 501(a)(4) of the act for any particular use, unless that use is "listed" (approved) pursuant to a regulation issued under section 706(b) of the act.

Congress did not provide in the amendments for a transition or phase-in period for the agency's new regulatory authority over color additives used in devices. For this reason, on the date of enactment of the amendments, any device in commercial distribution that contained an unlisted color additive that came in direct contact with the body for a significant period of time was technically adulterated within the meaning of section 501(a)(4) of the act. Although the act authorizes regulatory action against adulterated devices, FDA does not believe that Congress intended FDA to take enforcement action against devices containing an unlisted color additive immediately upon enactment of the amendments. In deciding whether to approve or deny approval of a PMA for a device that contains a color additive that is subject to section 706 of the act, however, FDA believes that it cannot ignore the requirement in section 706 of the act that an unlisted color additive used in or on the device be deemed unsafe. Furthermore, approval of such a PMA without regard to the requirements of section 706 would frustrate the intent of section 515(d)(2)(A) of the act, which requires FDA to deny approval of a PMA if "there is a lack of showing of reasonable assurance that [the] device is safe • • •."

44. One comment states that FDA had approved PMA's for at least two tinted contact lenses, even though the color additive used to color the lenses had not been listed for that use before the applications were approved. The comment argues that FDA's subsequent decision to subject color additives in class III contact lenses to the color additive, as well as the premarket approval, provisions of the act was unfair and raised very serious constitutional due process questions.

FDA notes that the color additive in question was listed for use to color contact lenses by a final rule published in the FEDERAL REGISTER of March 29, 1983 (48 FR 13020). As noted in paragraph 50 of this document, several other color additives have been listed for use to color contact lenses.

FDA acknowledges that it approved PMA's for two contact lenses tinted with a color additive that was not listed for use to color a contact lens when the applications were approved. After the first approval but before the second approval, FDA concluded that it could not refrain from applying the color additive provisions of the act to tinted contact lenses (see paragraph 43 of this document). In this circumstance, it was decided that the least unfair method of proceeding would be to complete action on the pending PMA without listing the color additive for use in the lens, and to enforce the color additive provisions with respect to future PMA's. FDA realized then, and realizes now, that subjecting different manufacturers of similar lenses to different requirements is undesirable. The agency chose that course as the lesser of two evils, believing then, as it does now, that it could not defend the continued processing of PMA's without regard to the legal requirements of the act.

FDA advises that it is developing a policy for implementing the color additive provisions of the act with respect to preamendments devices that contain color additives that come in direct contact with the body for a significant period of time. FDA also is developing proposed changes in the procedural regulations for color additives to govern regulation of color additives in devices. Appropriate opportunity for comment will be given interested persons when the agency proposes the policy and the procedures. FDA fully intends to ensure consistent regulatory treatment of all devices that contain color additives that are subject to section 706 of the act.

45. One comment points out that the definition of color additive in section 201(t) of the act (21 U.S.C. 321(t)) does not include dyes or pigments "added to a device." The comment then argues that FDA views the Congress' failure to amend the definition to include a reference to devices as an error that the agency may ignore in the interest of avoiding what it deems to be an illogical result. Another comment argues that colorants in tinted contact lenses are not color additives within the meaning of section 201(t) because the colorants are not capable of imparting color to the human body.

FDA disagrees with the comments. Section 201(t) defines a "color additive" as a substance "capable • • • of" imparting color "when added or applied to a food, drug, or cosmetic, or to the human body." A colorant used to tint a device satisfies the "capable of" test if it can impart color when it is added or applied to the human body, whether or not it can impart color to the body when it is used in a device. The second comment did not provide any evidence that colorants used to tint contact lenses are not capable of imparting color to the human body.

46. One comment argues that a colorant used in or on a device is not a "color additive" unless the colorant is capable of migrating from the device in such a manner and in such quantity to give rise to a toxicological concern.

FDA disagrees with the comment. The definition of "color additive" in section 201(t) of the act, which is discussed in paragraph 45 of this document, does not distinguish between (1) substances that meet the definition and migrate in such a manner and in such quantity to give rise to a toxicological concern and (2) substances that meet the definition and do not migrate in such a manner and in such quantity to give rise to a toxicological concern. A colorant used to tint a device is a color additive if the colorant can impart color when it is added or applied to the human body.

47. One comment states that colorants used in tinted contact lenses facilitate finding a dislodged or decentered lens, thus contributing to its medical function. The comment argues that colorants used in contact lenses should therefore be excluded from the definition of color additive in section 201(t) of the act.

FDA advises that a substance that meets the definition of color additive in section 201(t) of the act is a color additive unless FDA determines, by regulation, that the substance "is used (or intended to be used) solely for a purpose or purposes other than coloring." Thus, the fact that a substance used to color a contact lens also contributes to its medical function does not provide any basis for FDA to determine that the substance is not a color additive within the meaning of section 201(t) of the act.

48. One comment claims that FDA's interpretation of the term "direct contact" in section 706(a) of the act leads to an absurd, unjust, or unintended result, namely, the regulation under section 706 of color additives used to tint contact lenses and other devices. The comment argues that the phrase "direct contact for a significant period of time" does not contemplate situations in which a colorant, as used in a device, cannot come in contact with the body in any physiologically or toxicologically significant sense.

FDA disagrees with the comment. The plain language of section 706(a) of the act requires the agency to subject to the requirements of section 706 any color additive that is used in or on a device and that comes in "direct contact" with the body for a significant period of time, and nothing in section 706(a) or its legislative history suggests that Congress intended the term "direct contact" or "significant period of time" to comprehend physiological or toxicological significance.

FDA's interpretation does not imply a belief that color additives used to tint contact lenses and other devices

necessarily pose a health problem. The color additive provisions of the act are not intended to deal only with additives known to present a risk, but are designed, instead, to allow the agency to evaluate the safety of additives used in regulated products in a systematic way.

In FDA's view, tinted contact lenses involve the sort of use of a color additive in a device that was meant to be evaluated in accordance with the color additive provisions of the act. Contact lenses come in direct contact with the eye and are worn for prolonged periods of time every day. Whether and to what extent a lens' tint leaches out of the lens material in these circumstances is a matter of legitimate regulatory inquiry. Because the tint is a color additive, this inquiry is properly conducted under the color additive provisions of the act.

49. One comment argues that the phrase "significant period of time" in section 706(a) of the act must be interpreted logically to avoid an absurd result, namely, the regulation under section 706 of color additives in contact lenses and other devices, unintended by Congress. The comment claims that in the case of a device from which a colorant readily migrates, a significant period of time might be measured in minutes, whereas in the case of contact lenses and other devices (e.g., dentures) from which a colorant cannot migrate in significant amounts, the length of time during which the device may safely be placed in contact with the body may be practically limitless.

FDA agrees that a color additive used in or on a contact lens or any other device is not subject to section 706 of the act unless the color additive "comes in direct contact with the body of man * * * for a significant period of time" (section 706(a) of the act). For the reasons given in paragraphs 48 and 50 of this document, FDA has concluded that color additives used to tint contact lenses come in contact with the body in the manner and for the period of time contemplated by the statute, and, therefore, that

the safety of such additives for use in such lenses is required to be established in accordance with section 706 of the act and Part 70 of the regulations governing color additives (21 CFR Part 70). As explained in paragraph 51a of this document, however, a color additive used to tint a contact lens is not subject to the requirements of section 706 if there is a nontinted barrier impermeable to the color additive between the "colored" portion of the lens and every surface of the lens that comes in direct contact with the body, or the color additive is otherwise imprisoned within the lens in such manner that all of the color additive is and remains below every surface of the lens that comes in such contact.

FDA notes that no data concerning the migration or safety of colorants used to tint contact lenses or any other devices were included in or submitted with the comment.

50. Many comments state that color additives have been used in contact lenses for many years without any known adverse effects and that FDA therefore should have included tinted lenses in the proposed rule.

Because FDA is withdrawing the proposed rule, the question whether to include tinted lenses in any reclassification is moot. FDA advises, however, that regardless of the classification or regulatory status of tinted contact lenses, FDA believes that as such lenses are currently fabricated, the color additives used to tint the lenses are added to the lenses in such a way that at least some of each color additive will come in direct contact with the eye when the lenses are worn. In addition, the lenses are intended to be placed on the eye for several hours each day for 1 year or more. Thus, the color additives come in direct contact with the body for a significant period of time and, therefore, are subject to section 706 of the act. FDA notes that since publication of the proposed rule, several color additives have been listed for use in contact lenses (see, e.g., 48 FR 31374 (July 8, 1983); 48 FR 22705 (May 20,

1983); 48 FR 13020 (March 29, 1983)). FDA emphasizes, however, that as discussed in paragraph 51a of this document, any person submitting a PMA for a tinted lens may demonstrate in the application that the dye or pigment used to tint the lens does not come in direct contact with the body for a significant period of time and, thus, is not subject to section 706 of the act.

FDA agrees that tinted contact lenses have been marketed for many years. The lack of reports of adverse effects associated with such lenses does not, however, show that color additives are safe for use in tinting contact lenses. Indeed, because DEN is not comprehensive (see paragraph 6 of this document) and there currently are no reporting requirements applicable to all tinted lenses, the lack of reports of adverse effects does not and cannot establish that color additives are safe for tinting contact lenses.

Under section 706(b)(4) of the act, the so-called "general safety clause" for color additives, a color additive may not be listed for a particular use unless the data presented to FDA establish that the color additive is safe for that use. Although what is meant by "safe" is not explained in the general safety clause, the legislative history makes clear that this word is to have the same meaning for color additives as for food additives. (See. H.R. Rep. No. 1761, "Color Additive Amendments of 1960," Committee on Interstate and Foreign Commerce, 86th Cong., 2d Sess. 11 (1960).) The Senate report on the Food Additives Amendment of 1958 states that although proof of safety does require "proof of a reasonable certainty that no harm will result from the proposed use of an additive." S. Rep. No. 2422, "Food Additives Amendment of 1958," Committee on Labor and Public Welfare, 85th Cong., 2d Sess. 6 (1958).

FDA has incorporated this concept of safety into its color additive regulations. Under § 70.3(i), a color additive

is "safe" if "there is convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive." Under this standard, the lack of reports of adverse effects associated with tinted contact lenses could not establish the safety of the color additives used to tint the lenses, even if, as is not the case, DEN were comprehensive or reports of such effects associated with all tinted contact lenses were required to be submitted to the agency.

51a. One comment argues that the agency has no information that would indicate any significant leaching, migration, or elution of color additives from tinted contact lenses. Another comment claims to have evidence from leaching studies of a number of color additives used to tint contact lenses which demonstrates that an insignificant amount of the colors leaches from the lenses. The latter comment concludes, therefore, that a color additive in a tinted contact lens does not come in direct contact with the body for a significant period of time. Still another comment states that FDA had advised Congress that it did not intend to apply section 706 to a color additive used in or on a device if, even though the device comes in direct contact with the body for a significant period of time, there is a barrier impermeable to the color between the "colored" components of the device and the surface of the device that comes in direct contact with the body. The comment argues that the mechanism by which a colorant used to tint a contact lens is prevented from having such contact with the body—whether by imprisonment within a polymeric matrix or by virtue of a barrier—should not give rise to different regulatory consequences.

FDA's statutory responsibility for regulating color additives used in or on devices, including tinted contact lenses, is discussed in paragraphs 43 through 50 of this document. FDA notes that none of the comments provide any evidence to support the contention that, as tinted contact lenses are

currently fabricated, the color additives used to tint the lenses do not come in direct contact with the body (e.g., ocular tissues, tears, eyelids) for a significant period of time within the meaning of section 706(a) of the act. FDA advises, however, that even if a color additive does not migrate or elute from a contact lens in a "significant" amount, the color is nonetheless subject to section 706 of the act so long as the color additive comes in direct contact with the body for a significant period of time. In addition, the fact that a color additive is bound to a surface of a contact lens that comes in such direct contact does not mean that the color additive is not subject to the requirements of section 706 of the act. FDA has concluded that a color additive used to tint a contact lens is subject to the requirements of section 706 of the act unless there is a nontinted barrier impermeable to the color additive between the "colored" portion of the lens and every surface of the lens that comes in direct contact with the body, or the color additive is otherwise imprisoned within the lens in such manner that all of the color additive is and remains below every surface of the lens that comes in such contact. If a person submitting a PMA for a tinted contact lens demonstrates that such a barrier or other mechanism of imprisonment exists for the lens, the color additive is not subject to the requirements of section 706 of the act.

FDA advises that elution and migration studies may be used to support the safe use of a color additive in a tinted contact lens that contains no nontinted barrier impermeable to color or within which the color additive is not otherwise imprisoned and that is, therefore, subject to the requirements of section 706 of the act.

51b. One comment states that FDA should hold a public proceeding on the legal conclusion stated in the preamble to the proposed rule (47 FR 53405) that the color additive provisions of the act apply to tinted contact lenses.

FDA disagrees with the comment. The agency already has provided several opportunities for all interested persons to present their views concerning the application of sections 201(t) and 706(a) of the act to color additives used in or on contact lenses (see section I of this document), and in paragraphs 43 to 51a of this document, has summarized and responded to every significant comment received on tinted contact lenses.

K. Miscellaneous Matters

52. One comment suggests that contact lenses should be considered custom devices because lenses are ordered specifically for the patient named on the prescription. In addition, the lenses may need to be further modified by the practitioner to meet the individual needs of the patient and to perform to the satisfaction of the patient and practitioner.

Under section 520(b) of the act and § 812.3(b) of the regulations governing investigational use of devices, a custom device is a device that:

(1) Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist;

(2) Is not generally available to, or generally used by, physicians or dentists;

(3) Is not generally available in finished form for purchase or for dispensing upon prescription;

(4) Is not offered for commercial distribution through labeling or advertising; and

(5) Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet

the special needs of the physician or dentist in the course of professional practice.

For contact lenses to meet the custom device exemption, they are required to satisfy each of these requirements. Contact lenses do not meet the definition of a custom device because they fail to satisfy four and possibly five of the five requirements.

First, contact lenses do not qualify for the custom device exemption because they do not "necessarily deviate" from an appropriate premarket approval requirement or from devices generally available in order to comply with the order of an individual physician. FDA interprets the necessary deviation requirement to require that a device be sufficiently unique that clinical investigations would be impracticable. Such investigations using contact lenses are anything but impractical; scores of clinical investigations have been conducted by firms large and small, and FDA has approved dozens of contact lenses through the NDA and PMA processes.

Second, contact lenses are generally available to physicians.

Third, contact lenses are generally available in finished form for purchase or dispensing upon prescription.

Fourth, contact lenses are offered for commercial distribution through labeling or advertising.

Fifth, even so called "custom fitted" contact lenses, which are intended for use by an individual patient named in the order of a physician, and are to be made in a specific form for that patient, are merely variations within an approved range of powers and anterior and posterior surface contours and are to be fitted to a virtually unlimited number of patients in the course of professional practice.

For all these reasons, FDA has determined that contact lenses do not qualify for the custom device exemption. As

explained in paragraph 20 of this document, however, nothing in the act or the regulations forbids optical laboratories from modifying approved lenses to meet the needs of specific patients so long as the specifications of the lenses, as modified, remain within the specifications of the PMA's for the approved lenses.

53. Three comments submitted data showing that product liability claims and losses against contact lens manufacturers have been minimal and argue that these data demonstrate the safety of contact lenses. The data include summaries of three surveys of contact lens manufacturers. One survey covers about 50 manufacturers over a 5-year period and the other two surveys appear to cover approximately 100 manufacturers for an indefinite period. The survey summarizes indicate that total claims paid on behalf of the manufacturers surveyed were less than $20 thousand, over an indefinite period apparently spanning several years.

FDA believes that such information might suggest a history of apparent safety but does not constitute valid scientific evidence of the safety of rigid gas permeable lenses. The comments provide no information on the surveyed manufacturers' experience with any of the lenses proposed for reclassification or the number of the surveyed manufacturers' rigid gas permeable lenses in use; indeed, nothing in the comments reveals whether any experience with approved rigid gas permeable lenses is captured by the surveys.

FDA notes that the relatively small amount of money paid does not lead to the conclusion that contact lenses are safe. There is no way of determining from the surveys what percentage of users who could have filed claims did or did not do so. The reasons for not filing claims may be many and varied including the short-term, reversible nature of the injury, ignorance of user rights, ignorance of the cause of the injury, ignorance of the identity of the re-

sponsible person, or the cost of filing or prosecuting a claim.

Contact lens related injuries do occur with some frequency. For example, the U.S. Consumer Product Safety Commission National Electronic Injury Surveillance System (NEISS) (Ref. 3) estimates that approximately 20,000 contact lens related injuries were treated in emergency care facilities in the United States in 1981. This estimate is projected from a statistically representative sampling of institutions with emergency treatment departments. The sample includes approximately 500 documented admissions to such facilities for contact lens related injuries.

For all these reasons, no definitive conclusions can be drawn from the surveys.

54. One comment states that FDA should have referred the proposed reclassification to the Ophthalmic Section of the Ophthalmic; Ear, Nose, and Throat; and Dental Devices Panel (the Section), an FDA advisory committee, for a recommendation respecting the proposed change in classification. The comment argues that the proposal should have been referred in the exercise of sound regulatory discretion as well as a matter of law under section 513(e) of the act. The comment further argues that section 513(e) permits a limited exception to the requirement of advisory committee review only in situations in which the committee has previously reviewed the classification and its report has been subject to publication and public comment.

FDA disagrees with this comment. Section 513(e) of the act provides that FDA "may secure from the panel to which the device was last referred pursuant to [section 513(c) of the act] a recommendation respecting the proposed change in the device's classification." The plain language of section 513(e) of the act thus authorizes, but does not require, the referral requested by the comment,

and nothing in the act or its legislative history suggests that FDA's discretion in determining whether to seek a recommendation from any of its advisory committees is limited to situations in which the committee has made a previous recommendation concerning the classification of the device. In any event, as discussed in paragraphs 55 and 56 of this document, a petition to reclassify rigid gas permeable lenses from class III into class II was reviewed by the Section, which tentatively recommended that FDA reclassify the device into class II. Accordingly, no purpose would have been served by securing a recommendation from the Section respecting the proposed rule.

55. One comment states that FDA should include in the administrative record various documents and memoranda allegedly prepared by agency scientists following the tentative recommendation, on April 14, 1981, of the Section that contact lenses consisting principally of rigid plastic materials be reclassified from class III into class II, as requested by the Contact Lens Manufacturers Association (CLMA), in its reclassification petition dated March 2, 1981.

FDA advises that recognizing the potential public interest in any reclassification that might result from FDA's notice and comment rulemaking proceeding, CLMA's petition, amended petitions, supporting exhibits, the transcript of the Section meeting, FDA's analysis of the petitions, and comments received on the petitions following the Section meeting were placed on file under the docket number assigned to the November 24, 1981 notice of intent (Docket No. 81N-0352) in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. As explained in paragraph 57 of this document, however, CLMA's petition was mooted by FDA's decision to initiate this rulemaking proceeding. Accordingly, even

if they were relevant to this proceeding, neither the petition nor FDA's analysis of it would negate the conclusions, reached after full review of the evidence developed by the rulemaking, that rigid gas permeable lenses may not be reclassified. None of the other documents referred to in the comment is relevant to this proceeding.

56. One comment states that FDA should include in the administrative record a copy of the transcript of the April 14, 1981, open meeting of the Section at which it considered CLMA's petition to reclassify contact lenses consisting principally of rigid plastic materials from class III into class II. The comment argues that the deliberations of the Section, as reflected in the transcript of the meeting, are clearly relevant to the underlying questions of the safety and effectiveness of rigid gas permeable lenses and materials and, further, that the Section's tentative recommendation represents the unanimous and collective opinion of recognized experts that, as of April 1981, (a) class III was not necessary to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses meeting ANSI Z-80.6-1983; (b) there was no perceived need for mandated clinical testing for polymers falling within ANSI Z-80.6-1983; and (c) low priority was to be accorded to the development of any performance standard under section 514 of the act for these materials and, accordingly, they could be adequately regulated as class I devices.

As stated in paragraph 55 of this document, a copy of the transcript of the April 14, 1981, Section meeting has been filed in the docket file for the notice of intent to initiate this rulemaking proceeding. The agency notes, however, that this rulemaking proceeding was initiated by the agency on the basis of data it gathered, and that the agency chose not to exercise its authority under section 513(e) of the act to secure from the Section a recommendation respecting the proposed rule. FDA also notes that even if the Section's tentative recommendation and opin-

ions referred to in the comment were relevant to this proceeding, the tentative recommendation would not have been legally binding on the agency, and the opinions could not have established the safety or effectiveness of the lenses in question because opinions that are not based on valid scientific evidence within the meaning of § 860.7 do not constitute such evidence. In any event, even if it had granted CLMA's petition, FDA would have been required to proceed by informal rulemaking to reclassify contact lenses consisting principally of rigid plastic materials, as requested by CLMA (see paragraph 57 of this document).

57. One comment disagrees with FDA's conclusion that CLMA's petition to reclassify contact lenses consisting principally of rigid plastic materials from class III into class II was mooted by the agency's decision to initiate this rulemaking proceeding.

If FDA had decided to grant CLMA's petition, the agency would have been required under § 860.130(d) to publish in the FEDERAL REGISTER an order announcing FDA's intent to initiate a change in the classification of the device. Subsequently, the agency would have been required to proceed by informal rulemaking in accordance with section 513(e) of the act and § 860.130(c) as well as Part 10 of its administrative practices and procedures regulations (21 CFR Part 10). FDA did not initiate this reclassification proceeding on the basis of CLMA's petition because the petition did not contain sufficient information. FDA tentatively concluded, however, that there was adequate information outside the petition to justify initiating a reclassification proceeding. Because FDA issued on its own initiative the notice of intent that FDA would have been required to issue had CLMA's petition not been inadequate, the agency reaffirms its conclusion, stated in the November 24, 1981 notice of intent and in the preamble to the proposed rule (47 FR 53402), that the petition was moot.

58. A comment characterizes as unnecessarily and inappropriately inflexible the statement in the transitional notice (42 FR 63474) that "until a performance standard applicable to any [transitional] product listed above [including 'soft contact lenses'] is established and becomes effective, that product will continue to be subject to premarket approval." The comment states that the rationale for the statement in the transitional notice is not clear and points out that section 513(e) of the act provides that a regulation issued under that section changing the classification of a device from class III into class II may provide that such reclassification not take effect until the effective date of a performance standard established under section 514 of the act for the device. The comment argues that the statement is not applicable to the proposed rule to reclassify rigid gas permeable lenses because the proposal would have reclassified these devices from class III into class I.

For the reasons explained in sections II and III of this document, FDA has concluded that premarket approval is still necessary to provide reasonable assurance of the safety and effectiveness of rigid gas permeable lenses, and that FDA may not reclassify them into either class I or class II. Accordingly, there is no need to reexamine the transitional notice in the context of this rulemaking proceeding. FDA agrees that section 513(e) of the act permits, but does not require, that a regulation issued under that section take effect on the effective date of a performance standard established for the device that is the subject of the regulation.

59. One comment states that FDA should have prepared a regulatory impact analysis under Executive Order 12291 for the proposed rule and must prepare one for any final rule that the agency might issue.

FDA disagrees with this comment. Under Executive Order 12291, an agency is required to prepare a prelimi-

nary regulatory impact analysis if a proposed rule is determined to be a "major rule" as defined in the Order. Section 1(b) of Executive Order 12291 defines a "major rule" as any regulation that is likely to result in:

(1) An annual effect on the economy of $100 million or more;

(2) A major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or

(3) Significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic or export markets.

As stated in the preamble to the proposed rule (47 FR 53410), reclassification of rigid gas permeable lenses would have resulted in increased competition, decreased costs, and an increase in employment and also would have allowed small contact lens firms to compete in the world market. Therefore, the agency concluded that the proposed rule would not be a major rule within the meaning of the Order and that a regulatory impact analysis was not required to be prepared. Because there is no final rule in this proceeding, the requirements of the Order do not apply.

IV. REFERENCES

The following references have been placed on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, where they may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Tanaka, U.S. Patent No. 4,139,692, "Copolymer for Contact Lens, Its Preparation and Contact Lens Made Thereof," February 13, 1979.

2. Lippman, Jay I., "Gas Permeable Contact Lenses: An Overview," *Contact Lens*, Vol. 7, Number 1, 15-25, January-March, 1981.

3. National Electronic Injury Surveillance System, U.S. Consumer Product Safety Commission, National Injury Information Clearinghouse: Product Code 1676—Contact lenses, not specified, 1981; Product Code 1675—Contact lenses, soft, 1981; Product Code 1674—Contact lenses, hard, 1981.

List of Subjects in 21 CFR Part 886

Medical devices; Ophthalmic devices.

PART 886—OPHTHALMIC DEVICES

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to the Commissioner (21 CFR 5.10), the proposed rule on reclassification of daily wear spherical contact lenses consisting of rigid gas permeable plastic materials, which was published in the FEDERAL REGISTER of November 26, 1982 (47 FR 53402), is withdrawn and the rulemaking proceeding initiated by that proposal is terminated.

Dated: December 19, 1983

/s/ Mark Novitch
Mark Novitch
Acting Commissioner of
Food and Drugs

Certified to be a true copy of the original

/s/ Robin M. Spencer

APPENDIX E

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

21 CFR PART 886

[Docket No. 82N-0180]

PROPOSED RECLASSIFICATION OF DAILY WEAR SPHERICAL CONTACT LENSES CONSISTING OF RIGID GAS PERMEABLE PLASTIC MATERIALS

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) in issuing a proposed rule which, if adopted, would reclassify marketed daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials from class III (premarket approval) into class I (general controls). The proposal is based on new information respecting these devices. After reviewing any public comments received, FDA will promulgate a final rule reclassifying some or all of the lenses or will withdraw the proposed rule. Elsewhere in this issue of the FEDERAL REGISTER, FDA is publishing a separate proposal to reclassify certain marketed daily wear optically spherical hydrogel (soft) contact lenses from class III into class I.

DATE: Comments by (*insert date 30 days after date of publication in the FEDERAL REGISTER*).

ADDRESS: Written comments may be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

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National Center for Devices and
Radiological Health (HFK-300),
Food and Drug Administration,
8757 Georgia Ave.,
Silver Spring, MD 20910,
301-427-7175.

SUPPLEMENTARY INFORMATION:

I. BACKGROUND

A. History of the Proceedings.

On March 2, 1981, the Contact Lens Manufacturers Association (CLMA), Washington, DC 20006, submitted to FDA under section 513(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(e)) a petition to reclassify contact lenses consisting principally of rigid plastic materials from class III into class II (performance standards). FDA thereafter concluded that the petition did not meet all the requirements of § 860.123 (21 CFR 860.123) of the regulations governing reclassification of medical devices. FDA nonetheless determined that CLMA's objective was meritorious and tentatively concluded that daily wear spherical contact lenses consisting principally of rigid plastic materials should be reclassified from class III into class II. Under section 513(e) of the act and § 860.130(b)(1) (21 CFR 860.130(b)(1)) governing reclassification under section 513(e), FDA issued on its own initiative a notice of intent to initiate a change in the classification of such lenses (46 FR 57648; November 24, 1981). Because the agency issued on its own initiative the notice of intent that FDA would have been required to issue had CLMA's petition not been inadquate (see § 860.-130(d)), the agency concluded that the petition was moot and so stated in the November 24, 1981 notice.

The notice of intent invited public comment regarding any impact that reclassification of daily wear spherical contact lenses consisting principally of rigid plastic materials would have on manufacturers or distributors of contact lenses, on the costs or prices paid by consumers purchasing contact lenses, on governmental agencies or geographic regions, on whether the rulemaking would have significant or adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic or export markets. As of October 6, 1982, FDA had received 51 comments from ophthalmologists, optometrists, and contact lens manufacturers concerning lenses consisting principally of rigid plastic materials. Fifty comments favored reclassification into class II and are further discussed in section VII of this proposal. A comment argued that FDA should not reclassify daily wear spherical contact lenses made of all types of rigid plastic materials because the information available to the agency does not show that lenses made from all types of such materials are safe and effective for their intended use. FDA agrees with the comment. As discussed in section II of this proposal, the daily wear spherical contact lenses proposed for reclassification include only those lenses composed of certain rigid plastic materials.

In addition to the comments received on the notice of November 24, FDA also received comments on CLMA's petition. Two of these comments objected to any reclassification of these lenses if there is not a performance standard in effect. FDA has recognized some of these comments' substantive concerns in section VI, which invites public comment on this proposal.

B. The Statutory Scheme.

On May 28, 1976, the Medical Device Amendments of 1976 (the amendments) (Pub. L. 94-295), amending the Federal Food, Drug, and Cosmetic Act, became law. The

amendments established a comprehensive system for the regulation of medical devices intended for human use. One provision of the amendments, section 513 of the act, establishes three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of any device's safety and effectiveness. The three catgories are as follows: class I, general controls; class II, performance standards; class III, premarket approval. A device is in class I if the general controls authorized by or under the act are sufficient to provide reasonable assurance of the safety and effectiveness of the device (section 513(a)(1)(A)(i) of the act; 21 CFR 860.3(c)(1)). A class II device is a device for which general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, for which there is sufficient information to establish a performance standard to provide such assurance, and for which "it is therefore necessary to establish * * * a performance standard under section 514 [21 U.S.C. 360d] to provide reasonable assurance of its safety and effectiveness" (section 513 (a)(1)(B) of the act; 21 CFR 860.3(c)(2)). A device is in class III if the device cannot be classified into class I or class II and if, in addition, the device is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury. For a device in class III, premarket approval is or will be required in accordance with section 515 of the act (21 U.S.C. 360e) to provide reasonable assurance of the safety and effectiveness of the device (section 513(a)(1)(C) of the act; 21 CFR 860.3(c)(3)).

The amendments not only established a comprehensive system of device regulation, they also changed the definition of "device" in section 201(h) of the act (21 U.S.C. 321(h)) so that some products that previously were "new drugs" within the meaning of section 201(p) of the act

upon enactment of the amendments became "devices" under the revised definition in section 201(h).

Before passage of the amendments, FDA considered certain ophthalmic devices to be "new drugs" subject to section 505 of the act (21 U.S.C. 355), which forbids the marketing of such drug unless the agency has approved a new drug application (NDA) covering the drug, use, and labeling in question. To provide for the continuous regulation of these products—that is, products that previously were regulated as "new drugs" but now are defined as "devices"—Congress included in the amendments special transitional provisions (section 520(1) of the act (21 U.S.C. 360j(1)). The transitional provisions apply to any product that is a device (under the revised definition in section 201(h)) and that satisfies one or more of six criteria. Under one of these criteria (section 520(l)(1)(E)),

> (1) [a]ny device intended for human use— • • •
>
> (E) which the Secretary in a notice published in the Federal Register before the enactment data has declared to be a new drug subject to section 505 • • • is classified in class III unless the Secretary in response to a petition [for reclassification] • • • has classified such device in class I or II.

The transitional provisions further provide in section 520 (l)(3)(D)(i)

> (3) • • •
>
> (D)(i) • • • [A] device which is described in subparagraph • • • (E) • • • of paragraph (l) and which is in class III is required, unless exempt under subsection (g) [which governs device investigations] of this section, to have on and after sixty days after the enactment date in effect an approved application under section 515.

The provisions quoted above specifically provide that any device which FDA, by notice published in the FEDERAL REGISTER before enactment of the amendments, declared to be a "new drug" subject to section 505 of the act, is now classified in class III and, as such, is required either to have an approved premarket approval application (PMA) under section 515 of the act, or an investigational device exemption from such approval as provided for by section 520(g) of the act, unless the device has been reclassified by FDA into class I or II. Section 501(f)(1)(C) of the act (21 U.S.C. 351(f)(1)(C)) provides in relevant part that a device shall be deemed to be adulterated:

> (f)(1) If it is a class III device—
>
> (C) which was classified under section 520(l) into class III, which under such section is required to have in effect an approved application under section 515, and which does not have such an application in effect.

Thus, any transitional device that does not have the required approved PMA is adulterated and is, therefore, prohibited from interstate commerce under section 301(a) of the act (21 U.S.C. 331(a)).

In a notice published in the FEDERAL REGISTER of September 30, 1975 (40 FR 44844), FDA declared that all soft contact lenses, defined as all contact lenses consisting of polymers other than polymethyl-methacrylate (PMMA), e.g., cellulose acetate butyrate (CAB), polycarbonate, silicone, and hydroxyethylmethacrylate (HEMA), were "new drugs" subject to premarket clearance under section 505 of the act. The notice, which also included a proposed regulation to codify this position, states that since the introduction of soft contact lenses in the 1960's, FDA has regarded all contact lenses made from non-PMMA materials as "new drugs," and explains that the agency's decision to regulate them under section 505

> • • • was based on a recognition that new plastic materials that had not been shown to be safe or effective for use were being introduced for use in the manufacture of contact lenses. The introduction of these new materials led to new lens design and use, new manufacturing methods, and new methods for lens care. The Food and Drug Administration is concerned that the use of these contact lenses may result in serious eye damage if the new material of which they are composed is unsafe for use in the eye, if the user cannot feasibly care for the lenses, or if the highly complex procedures for the manufacture of these lenses are not carefully controlled to assure a product of uniform quality.

The notice went on to describe the types of studies that FDA concluded sponsors need to conduct to determine the safety of soft contact lenses and the factors that need to be taken into account to assess the adequacy of the procedures for manufacturing such lenses (see 40 FR at 44845; September 30, 1975).

As a result of the 1975 declaration and proposal, under the transitional provisions discussed above, non-PMMA contact lenses on the date of the amendments were automatically classified into class III without need for regulations or other action on the part of the agency. Nonetheless, in a notice published in the FEDERAL REGISTER of December 16, 1977 (42 FR 63472) (the transitional notice), FDA provided all interested persons further notice that various generic types of devices, including soft contact lenses, were class III devices subject to the premarket approval requirements of section 515 of the act. In addition, FDA affirmed the class III status of soft contact lenses in a notice published in the FEDERAL REGISTER of January 13, 1978 (43 FR 1966). The January 13, 1978 notice, which withdrew the 1975 proposed regulation but did not affect its declaration, stated:

> Those [contact lenses] that do not consist entirely of [PMMA] are • • • subject to the transitional provisions of section 520(l) • • • and therefore may not be commercially distributed without premarket approval.

C. The Legal Standard Governing Reclassification Under Section 513(e).

Section 513(e) of the act authorizes FDA to reclassify a device based on "new information" respecting the device. The term "new information" comprehends information developed as a result of a reevaluation of the data before the agency when a device was classified, as well as information not presented, not available, or not developed at that time. See, e.g., *Holland-Rantos* v. *United States Department of Health, Education, and Welfare,* 587 F.2d 1173, 1174 n. 1 (D.C. Cir. 1978); *Upjohn* v. *Finch,* 422 F.2d 944 (6th Cir. 1970); *Bell* v. *Goddard,* 366 F.2d 177 (7th Cir. 1966). In each of the cited cases, FDA had taken final action to withdraw approval of a marketing permit, rather than to effect a change that would relieve manufacturers of the obligation to obtain such a permit, as the proposal would do here. But the basis for both types of actions is the same, namely, a reevaluation made in light of changes in "medical science." *Upjohn* v. *Finch, supra,* 422 F.2d at 951. The agency believes, therefore, that the act permits a reevaluation based on such changes to support reclassification of a device, whether from class III into class I (or class II), class II into class I (or class III), or class I into class II (or class III).

The "new information" on which any reclassification is based is required to consist of "valid scientific evidence," as defined in section 513(a)(3) of the act and § 860.7(c) of the regulations. As specified in § 860.7(c)(1), FDA relies upon only such evidence to determine whether there is reasonable assurance that a device is safe and

effective. For the purposes of reclassification, the valid scientific evidence upon which the agency relies is required to be publicly available, i.e., may not be based on trade secret or confidential commercial information in PMA's (section 520(c) of the act), or on the detailed summaries of information respecting the safety and effectiveness of devices for which there are approved PMA's (section 520 (h)(3) of the act). FDA is required to make these summaries available to the public upon issuance of orders approving PMA's (section 520(h)(1) of the act).

To reclassify a device under section 513(e) of the act, the statute and the regulations require that the new, publicly available, valid scientific evidence of safety and effectiveness show (1) why the device should not remain in its present classification and (2) that the proposed reclassification will provide reasonable assurance of the safety and effectiveness of the device. In the case of a device classified in class III and proposed for reclassification into class I, the statue and the regulations require such evidence of safety and effectiveness to show (1) why the device should not remain in class III and (2) that general controls will provide reasonable assurance of the safety and effectiveness of the device.

Based on a careful review of new, publicly available, valid scientific evidence, FDA has tentatively concluded that daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials should be reclassified into class I (general controls). In FDA's judgment, the information discussed in this preamble shows that the devices are safe and effective for their intended use, and FDA believes that the general controls provisions of the act are sufficient to provide reasonable assurance of the safety and effectiveness of the lenses. The decision to propose reclassification into class I, rather than class II once a performance standard is in effect, is based on

FDA's belief that although sufficient information exists to establish a standard to provide reasonable assurance of the safety and effectiveness of daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials, there is no need to establish a performance standard to provide such assurance.

II. IDENTIFICATION OF THE DEVICE

For the purpose of reclassification, FDA is identifying this generic type of device as a daily wear spherical contact lens consisting of rigid gas permeable plastic materials. Such a lens is indicated for daily wear for the correction of myopia, hyperopia, or aphakia. Because the requisite publicly available safety and effectiveness data that FDA may use as the basis for reclassification apply only to a contact lens composed of a limited number of materials, a lens subject to this proposal is composed only of the following: (1) Cellulose acetate butyrate (CAB); or (2) Polyacrylate-silicone.

This proposal applies to any daily wear spherical contact lens that is made of the materials listed above and that has received premarket approval, and any contact lens FDA determines to be substantially equivalent to such approved lenses.

Contact lenses composed of CAB or polyacrylate-silicone are characterized as chemically and physically stable under the conditions of their intended use, optically clear, nontoxic, and nonallergenic. Such lenses do not support bacterial growth and are generally benign to corneal tissue. They provide gas permeability, wettability, or tear pumping action to ensure healthy maintenance of corneal tissue. There generally is no significant leaching of substances from contact lenses composed of CAB or polyacrylate-silicone. Those leachables present are of minimum concentration and are nontoxic and nonirritating.

Rigid lenses consisting of cross-linked PMMA are not included in this proposal because FDA has tentatively concluded that such lenses are PMMA lenses within the meaning of the 1975 proposal, and therefore do not require premarket approval. When FDA issued that proposal, certain lenses that were thought to consist entirely of PMMA, and which FDA regulated as devices rather than new drugs, actually were not pure PMMA. Such lenses consisted of PMMA and several ingredients (Refs. 1 and 2), including catalysts (e.g., benzoylperoxide), cross-linking agents, comonomers, or chain transfer agents.

In the 1978 notice that withdrew the 1975 proposal, FDA stated:

> The Commissioner of Food and Drugs recognizes that issues may arise as to whether particular contact lenses would have been regarded as devices or as new drugs before the Medical Device Amendments. These issues are relevant in determining whether particular contact lenses are subject to premarket approval by virtue of the transitional provisions. The Commissioner believes that such issues, if they arise, should be addressed on a case-by-case basis or in the future regulations classifying contact lenses that are not subject to the transitional provisions (43 FR 1966).

FDA cautions that, except for cross-linked PMMA lenses that FDA determines are substantially equivalent to PMMA lenses, cross-linked PMMA lenses remain in class III and may not be distributed in commerce without premarket approval. In at least one case, FDA already has determined that a cross-linked PMMA lens is substantially equivalent to a PMMA lens (Ref. 3). For the purpose of determining whether cross-linked PMMA lenses in general should be regarded as PMMA lenses, FDA will issue a FEDERAL REGISTER notice reopening the administrative record and the comment period in the rulemaking

proceeding to classify PMMA lenses, which FDA has proposed to classify into class II (47 FR 3694 at 3736; January 26, 1982). Cross-linked PMMA lenses will continue to be a class III device subject to the premarket approval provisions of the statute unless FDA concludes that they are PMMA lenses and includes them in the final regulation classifying PMMA lenses.

Multifocal (including bifocal), aspherical, and toric contact lenses consisting of rigid gas permeable plastic materials are excluded from this proposal because FDA is not aware of adequate new, publicly available, valid scientific evidence showing that such lenses are safe and effective.

This proposal would not exempt tinted contact lenses from the color additive provisions in section 706 of the act (21 U.S.C. 376). Regardless of whether a rigid gas permeable plastic contact lens is classified into class III, class II, or class I, a color additive in such a lens that comes in direct contact with the body of man or other animals for a significant period of time is subject to regulation under section 706. (See 21 U.S.C. 376.) Any rigid gas permeable plastic contact lens that bears or contains a color additive accordingly is deemed to be adulterated under section 501(a)(4) of the act (21 U.S.C. 351(a)(4)) and thus prohibited from commerce unless, among other things (1) there is in effect, and such additive and such use are in conformity with, a regulation issued under section 706(b) of the act (21 U.S.C. 376(b)) listing such additive for such use or (2) such additive and such use conform to the terms of an exemption which is in effect pursuant to section 706(f) of the act (21 U.S.C. 376(f)).

III. REASONS FOR THE PROPOSAL

To determine the proper classification of the device, FDA considered the criteria specified in section 513(a)(1)

of the act. For the reasons discussed below, FDA has tentatively concluded that the general controls authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration, listing, and premarket notification), 516 (banned devices), 518 (notification and other remedies), 519 (records and reports), and 520 (general provisions including current good manufacturing practice requirements) of the act (21 U.S.C. 351, 352, 360, 360f, 360h, 360i, 360j) are sufficient to provide reasonable assurance of the safety and effectiveness of daily wear spherical contact lenses composed of CAB or polyacrylate-silicone.

1. New, publicly available, valid scientific evidence shows that the device is safe and effective for its intended use. The safety of the device also is shown by the absence of reports in the literature of serious, irreversible adverse effects on health presented by the device. Additionally, FDA notes that no such alleged effects have been reported to the agency's Device Experience Network (DEN).

2. The materials that contact the eye that are used in the device have been shown to be generally acceptable and to have known acceptable properties (Ref. 4). FDA's guidelines for toxicological, microbiological, and clinical evaluation of contact lenses and guidelines for contact lens manufacturing controls have been used by contact lens manufacturers for premarket clearance submissions (NDA's and PMA's) for the past 10 years (Ref. 5). A guideline developed by the former U.S. Interagency Regulatory Liaison Group describes test methods used to evaluate acute eye irritation (Ref. 6). Autian provides additional information on toxicological evaluation of biomaterials (Ref. 7) and Galin, et al., provide data on the use of tissue culture methods to test toxicity of ocular plastic materials (Ref. 8).

3. Current methods of chemical and physical analysis of materials allow determination of purity, structure, and

solubility of polymers, and the presence of trace elements (Ref. 7).

4. FDA believes that clinically significant properties and design characteristics of the device include total effective oxygen transport to the cornea by gas permeability and tear pumping; degree of surface wetting; dimensional stability under normal use, including cleaning and handling; optical transmission and refractivity; tensile and flexural strength and recovery from deformation; and abrasion and impact resistance. By including in this proposal only those rigid daily wear spherical contact lenses that consist of CAB and polyacrylate-silicone and that have received premarket approval and any contact lenses found by FDA to be substantially equivalent to such approved lenses, the agency believes the clinically significant properties and design characteristics listed above will be assured, should any of the lenses proposed for reclassification actually be reclassified.

5. FDA recognizes that all the general controls provisions of the statute apply to the device. Of particular importance, however, are the premarket notification procedures (21 CFR 807.87), which enable FDA to determine substantial equivalence, and the current good manufacturing practice (GMP) regulations (21 CFR Part 820), which apply to all devices. To establish that a new lens is substantially equivalent to any currently marketed lens that is reclassified, the manufacturer should be prepared to demonstrate substantial equivalence in terms including, but not limited to, design; composition; optical transmission (and homogeneity) and index of refraction; and other physical properties including oxygen permeability, chemical and physical stability, tensile and flexural strength; biocompatibility, including cytotoxicity, eye irritation, and nonsupport of bacterial growth; impurites; leachables; heavy metal levels; preservative uptake and release; and lens care/cleaning regimen compatibility. All

these properties relate to the basic characteristics of the device. To establish substantial equivalence, the manufacturer also will be required to demonstrate compliance with 21 CFR Part 820. FDA may permit such a showing to be made in a premarket notification submission containing a detailed description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the device and how such methods, facilities, and controls meet the requirements of the regulations.

In the transitional notice, FDA stated that some of the types of devices formerly regarded by the agency as new drugs—including soft contact lenses—and for which premarket approval is required "may be adequately regulated under performance standards." (See 42 FR at 63474; December 16, 1977.) In that notice, FDA also stated: "[U]ntil a performance standard applicable to any [of certain specified products, including soft contact lenses] is established and becomes effective, that product will continue to be subject to premarket approval." A performance standard for rigid gas permeable contact lenses could address, among other things, biocompatibility, oxygen permeability, polymer ratios and other specifics of composition, assays for the purity of materials, leaching, biodegradability, configuration and design, and cleaning and disinfection. FDA expressed concerns about some of these variables and the need for manufacturing controls to assure uniform quality in the 1975 notice declaring such lenses as new drugs. (See sction I.B. above).

This proposal to reclassify daily wear spherical contact lenses composed of CAB or polyacrylate-silicone into class I, rather than into class II upon the effective date of a performance standard promulgated in accordance with section 514 of the act, is based on FDA's tentative conclusion that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of such lenses. FDA believes that sufficient information exists to establish

a section 514 standard to provide reasonable assurance of the safety and effectiveness of the device; however, FDA does not believe it is necessary to establish such a standard to provide such assurance.

FDA notes that in 1975, when the agency declared as new drugs all contact lenses that did not consist entirely of PMMA, there was relatively little publicly available information about, or experience with, non-PMMA lenses, and the materials from which such lenses were being manufactured had not been shown to be safe or effective for use. As discussed in section IV of this notice, since the late 1970's rigid gas permeable contact lenses have been marketed in substantial numbers in this country, and they have been shown to be safe and effective. FDA believes that this marketing experience reflects such lenses' basic biocompatibility and nonbiodegradability, and the feasibility of cleaning and disinfecting them. Application of the premarket notification requirements set out in section 510(k) of the act (21 U.S.C. 360(k) and § 807.87 of the regulations, including the requirement that manufacturers demonstrate substantial equivalence to reclassified marketed lenses with respect to design, composition, optical properties, biocompatibility, and other basic characteristics of the device referred to earlier in this section of the preamble, will enable FDA to ensure that only daily wear spherical rigid gas permeable contact lenses that are safe and effective will be marketed. The GMP regulations require all manufacturers to prepare and implement quality assurance programs intended to assure that devices will be of uniform quality, safe, effective, and otherwise in compliance with the act. Application of the GMP regulations will enable FDA to ensure that only daily wear spherical rigid gas permeable contact lenses of uniform quality are marketed. For all of these reasons, FDA believes that a performance standard is not necessary to assure biocompatibility, nonbiodegradability, or the other composition and design characteristics referred to above, or to ensure the manufacture of lenses of uniform quality.

IV. SUMMARY OF THE DATA ON WHICH THE PROPOSED RECLASSIFICATION IS BASED

A. Preclinical Data.

The first patent for a PMMA contact lens was granted in 1950 (Ref. 10). In recent years, other rigid plastic materials have been developed and used for contact lenses. The first CAB lens was approved by FDA in 1978. A polyacrylate-silicone lens was approved in 1979. At present, approximately 1 million people in the United States wear contact lenses consisting of CAB or polyacrylate-silicone (Ref. 11). Since the introduction of such lenses, few reports of adverse reactions or complications have been described in the literature, or submitted to FDA through its DEN. FDA recognizes that the DEN is wholly voluntary and, as such, cannot reasonably be expected to receive reports of all adverse reactions or complications from rigid gas permeable contact lenses composed of CAB or polyacrylate-silicone. FDA believes, however, that the reports received through the DEN are representative of some of the types of adverse reactions or complications that may result from the use of such lenses. As of September 1982, the DEN contained three reports of adverse reactions to such lenses, and three reports of adverse reactions to lenses whose type could not be identified (Ref. 12). None of these reports indicated that any serious, irreversible adverse effects had occurred as a result of CAB or polyacrylate-silicone rigid contact lens wear.

Corneal tissue integrity and wearer comfort are important considerations in the safe use of daily wear contact lenses. The lack of oxygen permeability of PMMA lenses, if not offset by tear pumping action, has been linked to corneal edema and subsequent wearer discomfort (Ref. 13). In fact, a study by Mandell (Ref. 14) indicates that even a carefully designed PMMA contact lens fitted by the most skilled practioner may cause some level of edema. In contrast, the gas permeability of contact lenses con-

sisting of CAB or polyacrylate-silicone copolymers allows direct transmission of oxygen to corneal tissue (Refs. 15 and 16). Additional advantages ascribed to rigid gas permeable contact lenses include greater wearer comfort and less probability of corneal abrasion from physiological insult than have been experienced with PMMA contact lenses (Ref. 13).

Contact lenses composed of CAB are chemically stable, optically clear, nontoxic, and nonallergenic (Ref. 17). The edge thickness and contour of rigid plastic contact lenses, including CAB, are two important factors in determining tolerance by the patient (Ref. 18). Morris and Lowther measured the thickness of two types of CAB contact lenses (17 lenses in total) at different distances from the edge, and edge contours were viewed microscopically (Ref. 18). A difference in thickness and contour was found among CAB contact lenses produced by different manufacturers. This difference could affect contact lens comfort. Because the edges of contact lenses are made in standard shapes and not to patient specifications, adjustments in edge thickness and contour can be made after patient fitting, if needed (Ref. 19). These adjustments, which may include flattening the lens curve, thinning the front surface, or polishing the edge itself, are considered standard practice after patient fitting (Reg. 19). The surface tension of CAB contact lenses is lower than that of PMMA contact lenses, thus facilitating wettability of the contact lens surface (Ref. 17). For PMMA lenses to exhibit wettability comparable to that of CAB lenses, PMMA lenses need to be treated with wetting solutions (Ref. 17).

Polyacrylate-silicone copolymer contact lenses consist of complex siloxanyl methacrylate polymers (Refs. 20 and 21). Such lenses contain PMMA for rigidity and polymerized silicone for oxygen permeability (Refs. 20 and 21). They are characterized as optically clear, chemically stable, nontoxic, nonallergenic, oxygen permeable, wettable, and

scratch and break resistant (Refs. 20 and 21). As noted for CAB contact lenses, variations in the edge thickness and contour of polyacrylate-silicone lenses do occur, even among contact lenses produced by an individual manufacturer (Ref. 18). FDA believes this concern can be addressed through standard adjustments or edge modifications after patient fitting (Ref. 19). Design specifications of these contact lenses include specifications for diameter, edge lift, center and edge thickness, lens flexure, and lenticular construction (a carrier rim surrounding the central optical zone) and have been described (Ref. 21). The availability of practical fitting information to ophthalmologists and optometrists increases the likelihood of effective fitting and wearing. This information can be specified in labeling and assured through general controls.

B. Clinical Data On Specific Rigid Gas Permeable Lenses.

1. *Cellulose acetate butyrate (CAB).* Kline and DeLuca (Ref. 22) studied the clinical response of 100 randomly selected myopic patients who had been fitted with CAB contact lenses. The purpose of the study was to evaluate the advantages and disadvantages of CAB lenses. The lenses used in the study had an index of refraction of 1.475. The average center thickness was 0.20 millimeter (mm) and average edge thickness was 0.15 mm. The optic zone was 1.4 mm less than the diameter. There were three peripheral curves 1.5 mm progressively flatter than the base curve. The diameters used ranged from 9.2 mm to 10.8 mm.

Of the 100 myopic patients, 52 were female and 48 were male. Patients ranged from 16 to 41 years of age. Seventy-five of the 100 patients had been unsuccessful in previous attempts to wear PMMA or hydrogel (soft) contact lenses, and 25 patients were first-time contact lens wearers. The flattest keratometry readings ranged from 41.75 to 50.00 diopters. Eight hours of wearing time was intended to be

reached within 1 week beginning with 3 hours on the day of dispensing.

Criteria for success included an assessment of visual acuity, subjective response, corneal physiology, and lens performance. Spectacle blur was assessed by measuring visual acuity with the spectacle prescription after removal of lenses. Patients were considered successful wearers if they experienced comfort, a minimum wearing time of 8 hours a day, visual acuity of 20/25 or better, no corneal edema, no vascularity, no significant bulbar conjunctival injection, no significant corneal staining, no increase in follicular hypertrophy of the superior palpebral (upper eyelid) conjunctiva, and no spectacle blur.

Of the 100 patients studied, 79 were successful wearers, while 21 were unsuccessful and discontinued use of the CAB lens. Of the 75 patients who had been unsuccessful PMMA or hydrogel (soft) contact lens wearers, 57 patients (77 percent) were successful with CAB lenses and 18 patients (23 percent) were unsuccessful. Of the 25 patients who were first-time lens wearers, 22 patients (88 percent) were successful and 3 patients (12 percent) were unsuccessful. Of the total of 21 patients who discontinued lens wear, 1 patient had spectacle blur, 2 patients had corneal edema and discomfort, 2 patients had fluctuating visual acuity and discomfort, and 16 patients had problems limited to discomfort. Corneal staining at the 3 and 9 o'clock positions of the eye occurred in 20 of 200 eyes. Mild bulbar conjunctival infection developed in 16 eyes, and moderate infection developed in 6 eyes. Overall, 72 patients reported good comfort with the lens; 8 patients reported fair comfort (lens awareness); and 20 patients had poor comfort and could not tolerate the CAB lens.

Over 50 percent of the patients were fitted "on-K," with the remaining almost equally divided between "steeper than K" and "flatter than K." Fitting relationship to K readings and lens diameter was analyzed to show possi-

ble correlation with comfort and successful wear. Although the results were not reported as statistically significant, lenses fitted "flatter than K" resulted in a higher percentage of poor comfort than the other two categories. Also, a higher percentage of failures were associated with lenses fitted "flatter than K." Success and failure were approximately the same for each diameter. Lenses were changed an average of 1.67 times on successful patients and 4.8 times on unsuccessful patients. No significant changes in base curves or powers of CAB lenses were found following lens wear.

The study showed that of 100 patients fitted with CAB lenses, 79 percent were successfully fitted for correction of myopia. The small incidence of spectacle blur with CAB lenses represents a significant advantage of this type of lens. Two patients with fluctuating vision had residual astigmatism requiring toric contact lenses. Reported glare ("watery" or "blurry" vision) was relieved by fitting larger diameter lenses. Discomfort was the major problem of patients adapting to CAB lenses. Of 107 eyes unsuccessfully fitted with previous lenses because of edema and discomfort, 80 were successfully fitted with CAB lenses (75 percent). This study, which was limited to myopic patients, showed a high rate of success with this CAB lens and strongly supports its safety and effectiveness for myopic correction.

Sigband (Ref. 23) reported on the clinical experience of 65 patients who previously had been unable to wear contact lenses and who were fitted with lathe-cut CAB contact lenses. The CAB lens used in the study ranged in power from -1.00 to -6.00 diopters; diameters were 8.8 mm, 9.2 mm, or 9.6 mm. Sixty of the 65 patients had been unable to wear PMMA lenses, and 5 had been unable to wear hydrogel (soft) contact lenses. The majority of patients (54) were myopic, 4 were hyperopic, and 7 were aphakic. Of the 65 patients fitted with CAB lenses, 7 were lost to followup. Of the remaining 58 patients, 48 patients (83

percent) were successful, and 10 patients were not successful wearers. Of the five patients who had been unable to wear hydrogel (soft) lenses, four patients (80 percent) were successfully refitted with CAB lenses. The seven patients lost to followup had previously been unsuccessful as PMMA lens wearers. Of the remaining 53 patients who had been unable to wear PMMA lenses, 44 patients (83 percent) were successfully refitted with CAB lenses. The primary cause of the 10 failures was lack of comfort (8 patients). One aphakic patient was unable to manipulate the lens, and one patient's lens developed deposits. Thirty-even patients wore the CAB lenses at least 2 years; of these, 11 wore their lenses for 3 years or more. This study showed that this CAB lens was safe and effective in 85 percent of 65 patients who were unable to wear hard or hydrogel (soft) contact lenses.

The use of CAB lenses in patients who had been unable to wear PMMA contact lenses also has been reported by Hales (Ref. 24), who conducted a study of 50 patients selected from a private clinical practice. Thirty-five of the 50 patients were female and 15 were male. Patients ranged in age from 12 to 57 years, with an average of 27 years of age. All eyes were normal (nondiseased), and all patients had previously discontinued use of PMMA contact lenses because of discomfort, poor vision, or corneal edema. Soft contact lenses had been tried by 10 patients; 7 patients had experienced discomfort or poor vision and had stopped wearing the lenses. Indications for use of the CAB lens included myopia, mild hyperopia, aphakia (lenticular lenses), astigmatism (prism ballast lenses), and presbyopia (bifocal lenses). The "flattest K" reading was used to calculate the base curve. Standard tables were used to determine diameter and thickness. Lens wear began with 4 hours on the first day and increased by 1 hour each day until the lenses could be worn all day. Criteria for evaluation of lens wear included comfort, excessive movement, tearing, excessive light sensitivity, flare, halo, pain, burn-

ing, itching, spectacle blur, unusual eye secretions, awareness of the lens, excessive blink rate, visual acuity, variable vision, blurred distant vision, reading problems, lens deposits, and problems with manipulating the lenses. Follow-up ranged from less than 2 months to more than 1 year.

Thirty of the 50 patients were successful wearers (60 percent); of these, 24 were myopic, 3 were hyperopic, and 3 were aphakic. Twenty patients (40 percent) discontinued lens wear; 16 were myopic and 4 were hyperopic. Of 99 eyes studied (50 patients), 78 eyes (79 percent) had the same visual acuity with the PMMA and the CAB lenses. Seven eyes (7 percent) had better vision with the PMMA lenses and 14 eyes (14 percent) had better vision with the CAB lenses. With PMMA lenses, visual acuity was 20/30 or better in 87 of the eyes (88 percent); and with CAB lenses, in 97 of the eyes (98 percent). Only 2 eyes had vision worse than 20/30 with the CAB lenses.

No patient discontinued use of the CAB lens due to poor vision or lens imperfections. Of the 20 patients who discontinued use of CAB lenses, 15 patients did so because of discomfort and 5 because of diffuse central corneal edema. Of the latter five patients, all had Schirmer test results showing decreased tear production. No patient using the CAB lens complained of spectacle blur. CAB lenses were successfully replaced with new CAB lenses in 7 patients (14 lenses). Replacement was necessary primarily because of lens instability resulting in flattening of the base curve. All patients studied had been unable to wear PMMA contact lenses. However, 60 percent were able to be successfully fitted with CAB lenses. Failures with CAB lenses were associated with inadequate tear production and discomfort.

This study showed that the CAB lenses studied were both safe and effective for the correction of myopia, hyperopia, or aphakia in the majority of patients fitted who were unable to tolerate PMMA lenses. Because discomfort and

corneal edema were causes of failure for both CAB and previous PMMA lens wear and because some, but not all, persons unable to tolerate PMMA lenses were able to successfully wear CAB lenses in this and other studies (Refs. 22 and 23), FDA believes that an equivalent or higher rate of success can be expected in patients who have not experienced intolerance to PMMA contact lenses.

In a smaller clinical study of nine patients who were wearing PMMA contact lenses, Mandell (Ref. 25) reported decreased corneal edema when these patients were refitted with CAB lenses. The average corneal swelling was 6.65 percent with PMMA lenses and 2.35 percent with CAB lenses. This study supports the conclusions from previously cited studies that in certain patients rigid gas permeable CAB lenses are safer than PMMA lenses.

Garcia (Ref. 26) evaluated the safety and effectiveness of CAB lenses for extended wear in aphakia. The power of the lenses used in the study ranged from +7.0 to +21.5 diopters with an average of 14 diopters. The diameters ranged from 8.5 to 10.4 mm, with most having a -3.00 power lenticular carrier. Corneal astigmatism ranged from 0 to 5 diopters with an average of 1.6 diopters.

One hundred and two patients (139 eyes) were fitted with CAB lenses at the mean keratometry reading or steeper. Of these 102 patients, 98 patients (134 eyes) were followed for an average of 2 years. Of the 102 patients, 54 were male and 48 were female. Patients ranged from 43 to 88 years of age, with a mean of 64.2 years of age. Some patients who were initially considered for the study had no difficulty removing or inserting a lens and had no desire to attempt extended wear. These patients were excluded from the study, but it was noted that many of these patients occasionally left their lenses in overnight as a matter of convenience, suggesting high tolerance for this lens. The exact number of these patients was not stated.

All patients included in the study achieved visual acuity equal to or better than the best spectacle correction. Spectacle blur was present, but was two lines or less upon immediate removal of lenses. After several weeks, changes in corneal astigmatism ranged from -1.00 to +0.50 diopter with an average of -0.08 diopter. Of the 102 patients, 4 patients (5 eyes) were immediately unsuccessful in wearing the lens. Of these failures, one patient had decreased visual acuity and difficulty in recentering the lens when it slipped off the cornea; two patients (three eyes) had edema and blurred vision on arising; and one patient was described as "too nervous." The remaining successfully fitted 98 patients (134 eyes) were followed from 3 to 60 months with an average of 24.75 months.

At the conclusion of the study, a total of 17 patients (17 percent) with 22 eyes (16 percent) had discontinued extended wear. This number includes the four patients who were immediately unable to wear the lens. The reasons for failure included edema (four patients) discomfort and lack of tint causing difficulty in finding a decentered lens (four patients), excessive dislocations and lack of tint (three patients), cystic macular edema (one patient), poor fit (one patient), dusty environment (one patient), repeated conjunctivitis (one patient), nervousness (one patient), unknown (one patient). Topical medications (drops) for treatment of glaucoma in five patients (nine eyes) did not interfere with lens wear except for occasional dislocations when inserting the drops. Nine patients (14 eyes) with significant ocular problems in addition to aphakia were successfully fitted with these lenses. The additional ocular conditions included recurrent uveitis, Behcet's disease, postoperative staphylococcal endophalmitis, and wound dihiscence secondary to postoperative trauma. Lens removal for cleaning ranged from removal every 4 to 7 days to every 3 to 6 weeks. The accumulation of mucus and oily deposits on the lenses was a common problem and varied in severity. There were no cases of corneal vascularization.

Early in the study, conjunctival cultures were performed on a small group of patients. The exact number was not stated. There was no significant increase in bacteria flora.

This study showed that CAB contact lenses for extended wear were safe and effective for 80 percent of the aphakic patients included in the study. FDA believes that if these lenses can be safely and effectively worn on the eye continuously for days, weeks, or months, the same lenses can be expected to be safe and effective for a lesser period, such as for daily wear.

Another study examining effectiveness and corneal response to extended wear of CAB contact lenses in aphakia was reported by Kaplan and Trimber (Ref. 27). The CAB lenses used in this study were manufactured by thermocompression molding. Thirty patients (41 eyes), who ranged from 51 to 81 years of age with an average of 65.0 years of age, were fitted with the lens 6 weeks after cataract extraction. Patients who were able to tolerate the lens were allowed to wear it for extended periods of time. Most patients wore their lenses continuously for 1 to 2 months. All 30 patients (41 eyes) were able to wear CAB lenses for extended periods of time. Visual acuity with the lens was 20/20 or better in 17 patients, 20/25 or 20/30 in 19 patients, and 20/40 or 20/50 in 5 patients.

For each of the 30 patients (41 eyes) with extended wear CAB lenses, the corneal thickness was measured and compared to unoperated fellow eyes not wearing a contact lens, to aphakic eyes with spectacle correction not fitted for contact lenses, and aphakic eyes with daily wear CAB lenses. Corneal thickness of the 41 eyes averaged 0.550 mm. Fourteen of the 30 patients with extended wear CAB lenses had unoperated fellow eyes not wearing a contact lens. In these patients, the corneal thickness of eyes with extended wear CAB lenses averaged 0.548 mm; the fellow eyes measured an average of 0.515 mm. The average corneal thickness of the eyes of 25 aphakic patients with

spectacle correction not fitted for contact lenses was 0.525 mm. The eyes of 13 aphakic patients with daily wear CAB lenses had an average corneal thickness of 0.538 mm. Previous studies of a normal population and those with extended wear soft contact lenses showed an average corneal thickness of 0.518 mm (Ref. 28) and 0.570 mm (Ref. 29), respectively. The extended wear CAB lenses used in this study produced minimal effects on corneal thickness while providing an effective correction of visual acuity for aphakic patients. FDA believes that this study shows that this lens was safe and effective for extended wear in aphakic patients and that this lens could be expected to be safe and effective for daily wear in aphakics.

FDA has tentatively concluded that these studies constitute valid scientific evidence demonstrating the safety and effectiveness of all marketed daily wear spherical CAB lenses.

2. *Polyacrylate-silicone copolymer.* Poster (Ref. 30) followed for 3 months 115 patients fitted with polyacrylate-silicone contact lenses. The lens used in this study was designed to allow the periphery and peripheral portion of the outer optical zone to align with the cornea. The center thickness of the lens was 0.07 mm. The geometry of the posterior surface of the lens, which contained secondary and tertiary curves, was used to determine lens positioning.

Of the 115 patients, 87 were female and 28 were male. Patients ranged from 10 to over 60 years of age. Of the 115 patients, 65 patients (56.5 percent) had been unsuccessful wearers of PMMA lenses because of limitations of wearing time and problems with comfort, edema, and staining, and 21 patients (18.3 percent) had been successful with PMMA lenses. Twelve patients (10.4 percent) had been unsuccessful with hydrogel (soft) contact lenses, and four patients (3.5 percent) had been successful with soft lenses. Thirteen patients (11.3 percent) were first-time contact lens wearers. Patients with diseased eyes, with the excep-

tion of patients with keratoconus, and patients with a history of allergic reactions to contact lenses or solutions, were excluded from the study.

The evaluation of a successful fit included lens performance, over-refraction, visual acuity, comfort, lens positioning, physiological responses, and the ability to wear the lens for at least 10 hours per day with no significant symptoms or adverse physiologic responses. The criteria for a well-fitted lens included minimal apical clearance with alignment of the peripheral curves and peripheral portion of the optical zone. The lenses used in this study ranged in power from plano to -10.50 diopters, with the majority ranging from -1.25 to -6.75 diopters. Excluding 5 keratoconus patients, base curves ranged from 7.20 mm to 8.10 mm. Most patients were fitted within ±0.15 mm of the flattest keratometry reading.

Of the 115 patients fitted with the lenses, 104 patients (90.4 percent) were successful. Of the 11 unsuccessful wearers, 5 were not followed up (several were having difficulty in adapting); 4 were switched to another lens material (reason not stated); and 2 had a history of corneal problems from previous PMMA lens wear. Good or excellent comfort was reported at 98.5 percent of all visits. Minimal symptoms, which ceased after the first weeks of wear, included some burning or itching (five patients), mild halos (one patient), mild injection (four patients), dryness (two patients), staining (five patients), and mild edema (two patients). Staining from PMMA lens wear was resolved or decreased with use of the polyacrylate-silicone lens in four patients. In addition, several patients (number not stated) with significant corneal distortion including extensive edema, edematous corneal formations, and central corneal clouding, returned to a more physiologically normal corneal curvature.

The polyacrylate-silicone lens used in this study was effective in 90.4 percent of myopic patients studied. No

serious adverse physiological responses occurred, even among unsuccessful wearers. Thus, the lens also was shown to be safe in patients in the study.

Sarver, et al. (Ref. 31), reported on a study of 46 patients who had been unable to wear PMMA lenses and who were fitted with polyacrylate-silicone lenses. The 46 patients, who were fitted with the lenses over an 18-month period, ranged from 17 to 55 years of age, with a mean age of 51 years. Thirty-eight were female and eight were male. In 40 patients (87 percent), the reasons for failure with PMMA lenses included significant edema associated with discomfort, spectacle blur, and limited wearing time; 6 patients (13 percent) experienced discomfort or flare without edema.

Forty-two patients were fitted with polyacrylate-silicone lenses having the same dimensions as their best-fitting PMMA lenses. The remaining four patients were fitted with larger diameter lenses to reduce flare and edge reflections. The mean center thickness of the lenses used in this study was 0.14 mm. The powers of the spherical lenses ranged from -8.50 to 5.75 diopters, with a mean of -3.44 diopters. The cylindrical corrections ranged from plano to -3.25 diopters, with a mean of 0.90 diopter. The flat keratometry reading ranged from 39.25 to 46.00 diopters, with a mean of 43.04 diopters.

Of 46 patients (92 eyes), 31 patients (67 percent) were successful when considering all of the following criteria: wearing time, comfort, vision, corneal edema, staining, ocular injection, and patient appearance. Thirteen patients (28 percent) were unsuccessful. The response of two patients was unknown. The 13 unsuccessful patients had persistent discomfort in spite of lens modifications such as base-curve changes and edge refinishing. These patients had failed in attempts to wear PMMA lenses due to edema and discomfort; however, discomfort alone (not edema)

was identified as the reason for the unsuccessful use of the polyacrylate-silicone lens. No significant corneal edema was observed in any patient fitted with the lenses. Vascularization developed in three patients (no other details stated), and small amounts of central corneal staining developed in three others. Most patients reported decreased spectacle blur with the polyacrylate-silicone lens when compared to the PMMA lenses.

In 5 patients selected at random from the original 46 patients, corneal thickness was measured during an 8-hour wearing period with each of the polyacrylate-silicone lenses and the PMMA lenses of the same dimension. Measurements with each of the two lens types were made a week apart after weeks (number not stated) of wearing time. After 4 hours of wear, the mean increase in corneal thickness was 0.4 percent for polyacrylate-silicone lenses and 3.6 percent for PMMA lenses. After 8 hours, slight thinning of the cornea occurred with the polyacrylate-silicone lens, showing a mean increase of -0.2 percent; the mean increase with PMMA lenses was 3.6 percent.

Visual acuity was the same with the polyacrylate-silicone lenses as with PMMA lenses. This study, which was intentionally biased by the selection of patients who had failed with PMMA lenses, showed that the polyacrylate-silicone lens was safe and effective for the correction of myopia or hyperopia for the majority of patients studied. An absence of corneal edema and minimal corneal thickness increases were shown to be advantages of the polyacrylate-silicone lens used in this study. The major disadvantage of the lens was discomfort in some patients. Discomfort, however, had also occurred with the use of PMMA lenses.

FDA has tentatively concluded that these studies constitute valid scientific evidence demonstrating the safety and effectiveness of all marketed daily wear spherical polyacrylate-silicone lenses.

V. RISKS TO HEALTH

The risks associated with the use of the device include: (1) corneal abrasion that may occur from a chipped edge of a lens, a cracked lens, or poor lens design or fit; (2) corneal edema that may occur if lens design prevents adequate delivery of oxygen to the cornea; (3) corneal vascularization that may result from inflammation or as a result of corneal edema; (4) rainbows or halos around objects or blurring of vision that may occur if a lens is worn continuously or for too long a time; (5) excessive tearing, unusual eye secretions, and photophobia, the cause of which would have to be determined from examination of contact lenses and eyes; and (6) giant papillary conjunctivitis, the exact cause of which is unknown.

VI. PUBLIC COMMENT

FDA invites comments on all aspects of the proposal, but particularly on the following issues:

1. Do the data presented in this proposal constitute sufficient "valid scientific evidence" of safety and effectiveness to support reclassification of each marketed lens consisting of CAB or polyacrylate-silicone?

a. If not, what additional publicly available data are there to support reclassification?

b. If so, are general controls sufficient to provide reasonable assurance of the safety and effectiveness of the device?

c. If general controls are not sufficient to provide reasonable assurance of the safety and effectiveness of the device, is there sufficient information to establish a performance standard to provide such assurance?

d. If general controls are not sufficient, and there is sufficient information to establish a performance standard to provide reasonable assurance of safety and effective-

ness of the device, is a performance standard necessary to assure any of the lens properties or design characteristics that FDA has identified as "clinically significant" (see section III of the preamble) or to protect against any of the concerns raised in the 1975 notice declaring as new drugs all contact lenses consisting of polymers other than PMMA (see section I.B. of the preamble)?

e. Should any reclassification take effect (i) before or (ii) after such a standard has been established?

2. Is there publicly available "valid scientific evidence" to support reclassification of other than daily wear spherical lenses consisting of CAB or polyacrylate-silicone? For example, should (a) extended wear lenses, (b) toric lenses, or (c) other types of CAB or polyacrylate-silicone lenses be included in any reclassification? If so, what publicly available data are there to support reclassification of such other lenses?

3. With respect to the lenses proposed for reclassification, FDA has limited data on their use for the correction of hyperopia and in some cases aphakia. May FDA reclassify a lens for use in the correction of myopia, hyperopia, and aphakia based solely or primarily on data showing that the lens is safe and effective (a) for the correction of myopia? (b) for the correction of myopia and aphakia?

4. Does specifying the materials of which the lenses proposed for reclassification are principally composed adequately identify the lenses for the purpose of reclassification?

5. As discussed in sections III and IV of the preamble, the safety or effectiveness of a specific rigid gas permeable contact lens is affected by its specific composition, design, and various other clinically significant properties.

a. Do the data presented in this proposal provide sufficient "valid scientific evidence" of the safety and effec-

tiveness of CAB or polyacrylate-silicone lenses of any specific composition, design, or other characteristic?

b. If the data do not provide this evidence, may the identified lenses be reclassified because of FDA's tentative decision that the safety and effectiveness of composition, design, or other clinically significant properties of specific lenses can be assured through premarket notification submissions and substantial equivalence determinations?

6. Is there publicly available "valid scientific evidence" to support reclassification of rigid gas permeable contact lens accessories, including products for cleaning, disinfecting, wetting, and storage? If so, what publicly available data are there to support reclassification of such accessories?

VII. ECONOMIC IMPACT

As discussed in section I of this proposal, in the November 24, 1981 notice of intent FDA invited public comment on the economic impact of any reclassification of daily wear spherical contact lenses consisting principally of rigid plastic materials. Although none of the comments presented specific data on the economic impact, generally the comments from all groups stated that reclassification would benefit industry and consumers by enabling small firms to have access to newer and better contact lens materials. Thus, competition would increase, costs would decrease, and employment would increase in these small firms. Also, comments generally stated that the contact lens reclassification would allow small contact lens manufacturing firms to compete in the world market.

All future manufacturers of these devices would be relieved of the cost of complying with the premarket approval requirements in section 515 of the act. FDA recognizes that there may be an economic impact on manufacturers

marketing devices that are the subject of PMA's and that would be reclassified if this proposal were adopted, and invite comments regarding any such impact. The magnitude of the economic savings for manufacturers resulting from any reclassification would depend on the extent of premarket approval studies that industry would have conducted had these requirements remained in effect. This parameter cannot be reliably calculated to permit the quantification of the economic savings. Do any manufacturers or other interested persons have additional data on the economic impact of reclassification?

After considering the economic consequences of reclassifying the device as discussed above, FDA certifies that this proposal requires neither a regulatory impact analysis, as specified in Executive Order 12291, nor a regulatory flexibility analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96-354).

VIII. REFERENCES

The following materials are on file in the Dockets Management Branch (address above), where they may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

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5. FDA Contact Lens Guidelines on Toxicology, Microbiology, Clinical Manufacturing Evaluation and Controls, 1980.

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11. Memorandum of Telephone Conversation, Maria E. Donawa, M.D., and Irving Arons, Arthur D. Little, Inc., Sept. 13, 1982.

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List of Subjects in 21 CFR Part 886

Medical devices; Ophthalmic devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10), it is proposed that Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 886 (which was proposed in the FEDERAL REGISTER of January 26, 1982 (47 FR 3694)) by adding new § 886.5360, to read as follows:

PART 886—OPHTHALMIC DEVICES

§ 886.5360 Daily wear spherical contact lens consisting of rigid gas permeable plastic materials.

(a) *Identification.* A daily wear spherical contact lens consisting of cellulose acetate butyrate or polyacrylate-silicone is a device that is a curved shell with a spherical surface providing monofocal refraction to be worn by a patient directly on the globe or cornea of the eye to correct refractive errors and that is removed from the eye and cleaned daily. A lens subject to this section is limited to any daily wear spherical rigid gas permeable contact lens consisting of cellulose acetate butyrate or polyacrylate-silicone in commercial distribution as of the effective date of this regulation, or a lens that is determined by FDA to be substantially equivalent.

(b) *Classification.* Class I (general controls).

Interested persons may, on or before (*insert date 30 days after date of publication in the FEDERAL REGISTER*), submit to the Dockets Management Branch (address above) written comments on this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be

identified with the name of the device and the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: Nov. 5, 1982.

/s/ ARTHUR HULL HAYES, JR.
Arthur Hull Hayes, Jr.
Commissioner of Food and Drugs

Certified to be a true copy of the original

/s/ ROBIN M. SPENCER

APPENDIX F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

[Docket No. 81N-0352]

RECLASSIFICATION OF DAILY WEAR SPHERICAL CONTACT LENSES CONSISTING PRINCIPALLY OF HYDROXYETHYLMETHACRYLATE (HEMA) OR RIGID PLASTIC MATERIALS

AGENCY: Food and Drug Administration.

ACTION: Notice of intent.

SUMMARY: The Food and Drug Administration (FDA) is publishing notice of its intent to initiate proceedings to reclassify daily wear spherical contact lenses consisting principally of hydroxyethylmethacrylate (HEMA) or consisting principally of rigid plastic materials from class III (premarket approval) to class II (performance standards).

ADDRESS: Comments may be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:
George C. Murray,
Bureau of Medical Devices (HFK-460),
Food and Drug Administration,
8757 Georgia Ave.,
Silver Spring, MD 20910,
301-427-7940.

SUPPLEMENTARY INFORMATION: On January 16 and March 2, 1981, the Contact Lens Manufacturers Association (CLMA), Washington, DC 20006, submitted to FDA under section 513(e) of the Federal Food, Drug, and Cos-

metic Act (the act) (21 U.S.C. 360c(e)) petitions for the reclassification of contact lenses consisting principally of HEMA and contact lenses consisting principally of rigid plastic materials from class III to class II (81P-0084 and 81P-0085). The petitions were referred to the Ophthalmic Section of the Ophthalmic, Ear, Nose, and Throat; and Dental Devices Panel (the Section) for its recommendations regarding the proposed changes in classification. During an open meeting on April 14, 1981, the Section considered the petitions and tentatively recommended that HEMA contact lenses and rigid plastic contact lenses be reclassified from class III into class II. Further consideration by the Section was delayed pending, among other things, clarification and supplementation by CLMA of certain aspects of its petitions. On June 11, 1981, CLMA submitted amended petitions intended to address various concerns raised by FDA, and concurred in by the Section, during the April 14 meeting. Subsequently, Section members were provided copies of the amended petitions, and were contacted (by mail, by telephone, or in person) about them. The Section members recommended approval of both petitions, as amended.

FDA has completed its review of CLMA's submissions and has concluded that they are not adequate to satisfy all the requirements of § 860.123 (21 CFR 860.123) of the regulations governing reclassification of medical devices. The agency believes, however, that CLMA's objectives are meritorious and has tentatively concluded that daily wear spherical contact lenses consisting principally of HEMA or rigid plastic materials should be reclassified from class III to class II. Accordingly, FDA, pursuant to section 513 (e) of the act and § 860.130(b)(1) (21 CFR 860.130(b)(1)) of the regulations governing reclassification under section 513(e), is on its own initiative issuing this notice of intent to initiate changes in the classification of daily wear spherical HEMA contact lenses and daily wear spherical rigid

plastic contact lenses. In a future issue of the FEDERAL REGISTER, FDA will publish proposals to reclassify each of these generic types of lenses. In light of the agency's decision to initiate proceedings to effect the changes in classification sought by CLMA, FDA has concluded that the petitions are moot, and will not publish the Section's recommendations as provided in section 513(e) of the act and §860.130(c) of the regulations, or approve or deny the petitions, as provided in section 513(e) of the act and § 860.130(d) of the regulations. Nonetheless, because of the potential significance of, and public interest in, any reclassification that might result from FDA's notice and comment rulemaking proceedings, CLMA's petitions, amended petitions, supporting exhibits, the transcript of the Section meeting, FDA's analysis of the petitions, and comments received on the petitions following the meeting are on file under the docket number found in brackets in the heading of this notice, in the Dockets Management Branch, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

FDA invites public comment regarding any impact that reclassification of daily wear spherical contact lenses consisting principally of HEMA or rigid plastic materials would have on manufacturers or distributors of contact lenses, on the costs or prices paid by consumers purchasing contact lenses, on governmental agencies or geographic regions, on whether the rulemaking would have significant or adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic or export markets. Data and information supporting any such comments would be helpful. Comments are to be submitted to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket num-

ber found in brackets in the heading of this document. The agency will address the requirements of the Regulatory Flexibility Act and Executive Order 12291 entitled "Federal Regulation" when any proposal based on this notice of intent is published in the FEDERAL REGISTER.

Dated: Nov. 18, 1981.

/s/ WILLIAM F. RANDOLPH
William F. Randolph
Acting Associate Commissioner for
Regulatory Affairs

Certified to be a true copy of the original

/s/ ROBIN M. SPENCER

APPENDIX G

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

21 CFR PART 886

[Docket No. 82N-0180]

PROPOSED RECLASSIFICATION OF DAILY WEAR SPHERICAL CONTACT LENSES CONSISTING OF RIGID GAS PERMEABLE PLASTIC MATERIALS; REOPENING OF COMMENT PERIOD; ADVANCE NOTICE OF PUBLIC HEARING

AGENCY: Food and Drug Administration.

ACTION: Proposed rule; reopening of comment period; advance notice of public hearing.

SUMMARY: The Food and Drug Administration (FDA) is reopening the comment period in the rulemaking on the proposed reclassification of daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials from class III (premarket approval) into class I (general controls). FDA is reopening the comment period for the limited purpose of receiving additional information on certain specified issues. FDA also intends to hold a public hearing on this matter at a time and place to be announced in a future issue of the FEDERAL REGISTER.

DATE: Comments by (*insert date 30 days after date of publication in the FEDERAL REGISTER*).

ADDRESS: Written comments may be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Albert Van De Griek,
National Center for Devices and Radiological Health (HFK-402),
Food and Drug Administration,
8757 Georgia Ave.,
Silver Spring, MD 20910,
301-427-8162.

SUPPLEMENTARY INFORMATION: In the FEDERAL REGISTER of November 26, 1982 (47 FR 53402), FDA published a proposed rule to reclassify marketed daily wear spherical contact lenses consisting of certain rigid gas permeable plastic materials from class III (premarket approval) into class I (general controls), under section 513(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 306c(e)), based on new information respecting the devices. The proposal gave interested persons until December 27, 1982, to submit written comments. In the FEDERAL REGISTER of December 10, 1982 (47 FR 55497), FDA extended the comment period until January 26, 1983.

FDA has completed a preliminary review of the comments received during the comment period on the proposed rule. The comments submitted present contrasting views on some complex issues relevant to the proposed reclassification, but do not always provide the evidence necessary to support these views. FDA believes that resolution of the issues raised by the proposal and the comments would be facilitated by reopening the comment period for the limited purpose of receiving additional information on the specific issues discussed below in this document. FDA emphasizes that it is particularly interested in receiving clinical data, reports of relevant in vitro and nonclinical laboratory safety data, copies of articles from refereed journals, and other valid scientific evidence within the meaning of § 860.7

(c) of FDA's regulations governing classification of medical devices (21 CFR 860.7(c)), in support of any comments. All comments, data, and other evidence submitted in response to this document will be included in the docket file in this matter and will be available for public disclosure.

FDA recognizes that to reclassify the contact lenses at issue in this rulemaking from class III into class I, it must have new, publicly available, valid scientific evidence of safety and effectiveness demonstrating why the lenses should not remain in class III and why the "general controls" authorized by the act will provide reasonable assurance of the safety and effectiveness of the lenses. See Section 513(e) of the act and § 860.123 of the regulations governing reclassification of medical devices (21 CFR 860.123). Although this notice requests specific evidence showing why the lenses should not be reclassified, as well as evidence showing why they should be reclassified, FDA has not shifted the burden of proof to those opposing reclassification. FDA has concluded that additional evidence, both favorable and unfavorable to reclassification, is desirable to reach a sound decision on the complex issues involved in the rulemaking.

1. Some comments support the reclassification of a specific lens, or lenses composed of a specific family of materials, e.g., polyacrylate-silicone, stating that there are sufficient data to show that class I would provide reasonable assurance of the safety and effectiveness of the lenses, but do not include any data in support of their positions. Two comments include summaries of clinical studies, but do not provide complete data on the studies. To support or refute such comments, valid scientific evidence, within the meaning of § 860.7(c), particularly clinical data, should be submitted.

2. Many comments suggest that even if there is valid scientific evidence of the safety and effectiveness of the currently marketed lenses identified in the proposal, re-

classification into class I is inappropriate because the data necessary to determine whether a new rigid gas permeable contact lens is substantially equivalent to a reclassified lens will be of the type required to show safety and effectiveness in a premarket approval application. These comments claim that clinical trials will be necessary to demonstrate the safety and effectiveness of any new rigid gas permeable contact lens, even if the lens is made of materials specified in any final classification regulation and the specifications of the new lens are similar to those of a reclassified lens.

For example, some comments argue that small changes in polymers other than polymethyl-methacrylate (PMMA) or in the ratio of polymer constituents would change characteristics affecting the safety and effectiveness of the lens, including oxygen and glucose flux, friability, surface characteristics, and resulting vision, which, in the absence of clinical data, would not be detected. The comments also argue that lenses in which changes have been made in other ingredients, such as crosslinking agents, wetting agents, and colors, or changes in the manufacturing process, must be clinically tested to provide reasonable assurance of the lenses' safety and effectiveness. Other comments argue that clinical trials of new lenses are necessary to provide reasonable assurance of safety and effectiveness, because small changes in lens material or lens geometry may result in unpredictable lens fit or in poor tear lubricating and pumping action.

To support or refute the claim that clinical trials are always necessary to establish the safety and effectiveness of a gas permeable contact lens, valid scientific evidence within the meaning of § 860.7(c), including published studies, data from research and development programs, data on toxicity and biocompatability, or other specific information, should be submitted. FDA is particularly interested in receiving evidence that (a) demonstrates which,

if any, changes in lens formulation, geometry, or in manufacturing process require clinical testing to provide reasonable assurance of the safety and effectiveness of the resulting lens, and which changes do not require clinical testing; and (b) defines the necessary scope of any clinical testing that is required.

3. One comment stated that acrylate-silicone copolymers are nontoxic, stable, and gas permeable, and suitable for making contact lenses, if they are made from organosilicone monomers consisting of the "bone structure of acryloxy or methacryloxy connecting through the alkyl group to the silicone (siloxanyl groups)" with hydrogen, methyl groups, ethyl groups, phenyl groups, or cyclic groups attached to the silicone. If such monomers are copolymerized with a hardening monomer such as methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, cyclohexyl methacrylate, phenyl methacrylate, or *N*-vinyl pyrrolidinone, this comment argued, the copolymer can be sufficiently cross-linked to achieve the desired stability to produce a material suitable for making safe and effective gas permeable contact lenses, by incorporating various available cross-linking monomers on the market. To support or refute this claim, valid scientific evidence, within the meaning of § 860.7(c), should be submitted.

4. One comment stated that there have been very few product liability actions based on injuries resulting from the use of contact lenses. To support or refute this comment, evidence, e.g., insurance records, or data on the incidence of adverse effects from the use of the rigid gas permeable contact lenses identified in the proposal, should be submitted.

5. In the notice proposing reclassification, FDA stated that any final rule reclassifying the lenses would not exempt tinted contact lenses from the color additive provisions in section 706 of the act (21 U.S.C. 376), because regardless of the class the lenses are in, if a color additive

in such a lens comes in direct contact with the body for a significant period of time, the color additive is subject to regulation under section 706. On the basis of its experience, FDA believes that as most tinted contact lenses are fabricated, the color added to the lenses comes in direct contact with the human eye. Because such lenses are intended for daily wear for the lifetime of the lens, FDA believes that the contact is for a significant period of time. FDA has received several comments on the regulation of tints in contact lenses. These comments argue on various grounds that colors added to contact lenses are not subject to section 706. Evidence that the color added to any lens proposed for reclassification does not come in direct contact with the human eye should be submitted.

FDA believes that reopening the comment period to receive information on the issues specified in this notice will not delay final action on the proposed reclassification, but will expedite resolution of the complex issues involved in the rulemaking.

FDA has received two requests for a public hearing on the proposal to reclassify daily wear spherical contact lenses consisting of rigid gas permeable plastic materials and on other matters related to contact lenses. FDA is granting these requests insofar as they relate to reclassification. FDA will hold a public hearing before the Commissioner on the proposed reclassification under Part 15 of FDA's administrative practices and procedures regulations (21 CFR Part 15). FDA will announce the time and place of the hearing, the issues to be considered, and other details in a notice published in a future issue of the FEDERAL REGISTER.

Interested persons may, on or before (*insert date 30 days after date of publication in the FEDERAL REGISTER*), submit to the Dockets Management Branch (address above) written comments on this proposal. Two

copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the name of the device and the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: April 13 1983.

/s/ Arthur Hull Hayes, Jr.
Arthur Hull Hayes, Jr.
Commissioner of Food and Drugs

Certified to be a true copy of the original

/s/ Robin M. Spencer

APPENDIX H

STATUTES AND REGULATIONS INVOLVED

REGULATION OF MEDICAL DEVICES

SEC. 2. Chapter V is amended by adding after section 512 the following new sections:

"CLASSIFICATION OF DEVICES INTENDED FOR HUMAN USE

"Device Classes

"SEC. 513. (a)(1) There are established the following classes of devices intended for human use:

"(A) CLASS I, GENERAL CONTROLS.—

"(i) A device for which the controls authorized by or under section 501, 502, 510, 516, 518, 519, or 520 or any combination of such sections are sufficient to provide reasonable assurance of the safety and effectiveness of the device.

"(ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish a performance standard to provide such assurance, but because it—

"(I) is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

"(II) does not present a potential unreasonable risk of illness or injury,

is to be regulated by the controls referred to in clause (i).

"(B) CLASS II, PERFORMANCE STANDARDS.—A device which cannot be classified as a class I device because the controls authorized by or under sections 501, 502, 510, 516, 518, 519, and 520 by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, for which there is sufficient information to establish a performance standard to provide such assurance, and for which it is therefore necessary to establish for the device a performance standard under section 514 to provide reasonable assurance of its safety and effectiveness.

"(C) CLASS III, PREMARKET APPROVAL.—A device which because—

"(i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the controls authorized by or under sections 501, 502, 510, 516, 518, 519, and 520 are sufficient to provide reasonable assurance of the safety and effectiveness of the device and (II) cannot be classified as a class II device because insufficient information exists for the establishment of a performance standard to provide reasonable assurance of its safety and effectiveness, and

"(ii)(I) is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or

"(II) presents a potential unreasonable risk of illness or injury,

is to be subject, in accordance with section 515, to premarket approval to provide reasonable assurance of its safety and effectiveness.

If there is not sufficient information to establish a performance standard for a device to provide reasonable assurance

of its safety and effectiveness, the Secretary may conduct such activities as may be necessary to develop or obtain such information.

"(2) For purposes of this section and sections 514 and 515, the safety and effectiveness of a device are to be determined—

"(A) with respect to the persons for whose use the device is represented or intended,

"(B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and

"(C) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

"(3)(A) Except as authorized by subparagraph (B), the effectiveness of a device is, for purposes of this section and sections 514 and 515, to be determined, in accordance with regulations promulgated by the Secretary, on the basis of well-controlled investigations, including clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device, from which investigations it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device.

"(B) If the Secretary determines that there exists valid scientific evidence (other than evidence derived from investigations described in subparagraph (A))—

"(i) which is sufficient to determine the effectiveness of a device, and

"(ii) from which it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under

the conditions of use prescribed, recommended, or suggested in the labeling of the device,

then, for purposes of this section and sections 514 and 515, the Secretary may authorize the effectiveness of the device to be determined on the basis of such evidence.

"Classification; Classification Panels

"(b)(1) For purposes of—

"(A) determining which devices intended for human use should be subject to the requirements of general controls, performance standards, or premarket approval, and

"(B) providing notice to the manufacturers and importers of such devices to enable them to prepare for the application of such requirements to devices manufactured or imported by them,

the Secretary shall classify all such devices (other than devices classified by subsection (f)) into the classes established by subsection (a). For the purpose of securing recommendations with respect to the classification of devices, the Secretary shall establish panels of experts or use panels of experts established before the date of the enactment of this section, or both. Section 14 of the Federal Advisory Committee Act shall not apply to the duration of a panel established under this paragraph.

"(2) The Secretary shall appoint to each panel established under paragraph (1) persons who are qualified by training and experience to evaluate the safety and effectiveness of the devices to be referred to the panel and who, to the extent feasible, possess skill in the use of, or experience in the development, manufacture, or utilization of, such devices. The Secretary shall make appointments to each panel so that each panel shall consist of members with adequately diversified expertise in such fields as clinical

and administrative medicine, engineering, biological and physical sciences, and other related professions. In addition, each panel shall include as nonvoting members a representative of consumer interests and a representative of interests of the device manufacturing industry. Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this Act may be a member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

"(3) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, but not at rates exceeding the daily equivalent of the rate in effect for grade GS-18 of the General Schedule, for each day so engaged, including traveltime; and while so serving away from their homes or regular places of business each member may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703(b) of title 5, United States Code, for persons in the Government service employed intermittently.

"(4) The Secretary shall furnish each panel with adequate clerical and other necessary assistance.

"Classification Panel Organization and Operation

"(c)(1) The Secretary shall organize the panels according to the various fields of clinical medicine and fundamental sciences in which devices intended for human use are used. The Secretary shall refer a device to be classified under this section to an appropriate panel established or authorized to be used under subsection (b) for its review and for its recommendation respecting the classification of

the device. The Secretary shall by regulation prescribe the procedure to be followed by the panels in making their reviews and recommendations. In making their reviews of devices, the panels, to the maximum extent practicable, shall provide an opportunity for interested persons to submit data and views on the classification of the devices.

"(2)(A) Upon completion of a panel's review of a device referred to it under paragraph (1), the panel shall, subject to subparagraphs (B) and (C), submit to the Secretary its recommendation for the classification of the device. Any such recommendation shall (i) contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the recommendation is made, and (ii) to the extent practicable, include a recommendation for the assignment of a priority for the application of the requirements of section 514 or 515 to a device recommended to be classified in class II or class III.

"(B) A recommendation of a panel for the classification of a device in class I shall include a recommendation as to whether the device should be exempted from the requirements of section 510, 519, or 520(f).

"(C) In the case of a device which has been referred under paragraph (1) to a panel, and which—

"(i) is intended to be implanted in the human body or is purported or represented to be for a use in supporting or sustaining human life, and

"(ii)(I) has been introduced or delivered for introduction into interstate commerce for commercial distribution before the date of enactment of this section, or

"(II) is within a type of device which was so introduced or delivered before such date and is susbtantially equivalent to another device within that type,

such panel shall recommend to the Secretary that the device be classified in class III unless the panel determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. If a panel does not recommend that such a device be classified in class III, it shall in its recommendation to the Secretary for the classification of the device set forth the reasons for not recommending classification of the device in such class.

"(3) The panels shall submit to the Secretary within one year of the date funds are first appropriated for the implementation of this section their recommendations respecting all devices of a type introduced or delivered for introduction into interstate commerce for commercial distribution before the date of the enactment of this section.

"Classification

"(d)(1) Upon receipt of a recommendation from a panel respecting a device, the Secretary shall publish in the Federal Register the panel's recommendation and a proposed regulation classifying such device and shall provide interested persons an opportunity to submit comments on such recommendation and the proposed regulation. After reviewing such comments, the Secretary shall, subject to paragraph (2), by regulation classify such device.

"(2)(A) A regulation under paragraph (1) classifying a device in class I shall prescribe which, if any, of the requirements of section 510, 519, or 520(f) shall not apply to the device. A regulation which makes a requirement of section 510, 519, or 520(f) inapplicable to a device shall be accompanied by a statement of the reasons of the Secretary for making such requirement inapplicable.

"(B) A device described in subsection (c)(2)(C) shall be classified in class III unless the Secretary determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effective-

ness. A proposed regulation under paragraph (1) classifying such a device in a class other than class III shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for not classifying such device in such class and an identification of the risks to health (if any) presented by such device.

"(3) In the case of devices classified in class II and devices classified under this subsection in class III and described in section 515(b)(1) the Secretary may establish priorities which, in his discretion, shall be used in applying sections 514 and 515, as appropriate, to such devices.

"Classification Changes

"(e) Based on new information respecting a device, the Secretary may, upon his own initiative or upon petition of an interested person, by regulation (1) change such device's classification, and (2) revoke, because of the change in classification, any regulation or requirement in effect under section 514 or 515 with respect to such device. In the promulgation of such a regulation respecting a device's classification, the Secretary may secure from the panel to which the device was last referred pursuant to subsection (c) a recommendation respecting the proposed change in the device's classification and shall publish in the Federal Register any recommendation submitted to the Secretary by the panel respecting such change. A regulation under this subsection changing the classification of a device from class III to class II may provide that such classification shall not take effect until the effective date of a performance standard established under section 514 for such device.

"Initial Classification of Certain Devices

"(f)(1) Any device intended for human use which was not introduced or delivered for introduction into interstate commerce for commercial distribution before the date of the enactment of this section is classified in class III unless—

"(A) the device—

"(i) is within a type of device (I) which was introduced or delivered for introduction into interstate commerce for commercial distribution before such date and which is to be classified pursuant to subsection (b), or (II) which was not so introduced or delivered before such date and has been classified in class I or II, and

"(ii) is substantially equivalent to another device within such type, or

"(B) the Secretary in response to a petition submitted under paragraph (2) has classified such device in class I or II.

A device classified in class III under this paragraph shall be classified in that class until the effective date of an order of the Secretary under paragraph (2) classifying the device in class I or II.

"(2)(A) The manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition.

"(B)(i) Upon determining that a petition does not contain any deficiency which prevents the Secretary from making a decision on the petition, the Secretary shall refer the petition to an appropriate panel established or authorized to be used under subsection (b). A panel to which such a petition has been referred shall not later than ninety days after the referral of the petition make a recommendation to the Secretary respecting approval or denial of the petition. Any such recommendation shall contain (I) a sum-

mary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the petition was filed. In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the panel shall recommend that the petition be denied unless the panel determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. If the panel recommends that such petition be approved, it shall in its recommendation to the Secretary set forth its reasons for such recommendation.

"(ii) The requirements of paragraphs (1) and (2) of subsection (c) (relating to opportunities for submission of data and views and recommendations respecting priorities and exemptions from sections 510, 519, and 520(f)) shall apply with respect to consideration by panels of petitions submitted under subparagraph (A).

"(C)(i) Within ninety days from the date the Secretary receives the recommendation of a panel respecting a petition (but not later than 210 days after the filing of such petition) the Secretary shall by order deny or approve the petition. If the Secretary approves the petition, the Secretary shall order the classification of the device into class I or class II in accordance with the criteria prescribed by subsection (a)(1)(A) or (a)(1)(B). In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall deny the petition unless the Secretary determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. An order approving such petition shall be accompanied by a full statement of the reasons of the Secretary (and sup-

porting documentation and data) for approving the petition and an identification of the risks to health (if any) presented by the device to which such order applies.

"(ii) The requirements of paragraphs (1) and (2)(A) of subsection (d) (relating to publication of recommendations, opportunity for submission of comments, and exemption from sections 510, 519, and 520(f)) shall apply with respect to action by the Secretary on petitions submitted under subparagraph (A).

"Information

"(g) Within sixty days of the receipt of a written request of any person for information respecting the class in which a device has been classified or the requirements applicable to a device under this Act, the Secretary shall provide such person a written statement of the classification (if any) of such device and the requirements of this Act applicable to the device.

"Definitions

"(h) For purposes of this section and sections 501, 510, 514, 515, 516, 519, and 520—

"(1) a reference to 'general controls' is a reference to the controls authorized by or under sections 501, 502, 510, 516, 518, 519, and 520,

"(2) a reference to 'class I', 'class II', or 'class III' is a reference to a class of medical devices described in subparagraph (A), (B), or (C) of subsection (a)(1), and

"(3) a reference to a 'panel under section 513' is a reference to a panel established or authorized to be used under this section.

"GENERAL PROVISIONS RESPECTING CONTROL OF DEVICES INTENDED FOR HUMAN USE

"General Rule

"SEC. 520. (a) Any requirement authorized by or under section 501, 502, 510, or 519 applicable to a device intended for human use shall apply to such device until the applicability of the requirement to the device has been changed by action taken under section 513, 514, or 515 or under subsection (g) of this section, and any requirement established by or under section 501, 502, 510, or 519 which is inconsistent with a requirement imposed on such device under section 514 or 515 or under subsection (g) of this section shall not apply to such device.

"Custom Devices

"(b) Sections 514 and 515 do not apply to any device which, in order to comply with the order of an individual physician or dentist (or any other specially qualified person designated under regulations promulgated by the Secretary after an opportunity for an oral hearing) necessarily deviates from an otherwise applicable performance standard or requirement prescribed by or under section 515 if (1) the device is not generally available in finished form for purchase or for dispensing upon prescription and is not offered through labeling or advertising by the manufacturer, importer, or distributor thereof for commercial distribution, and (2) such device—

"(A)(i) is intended for use by an individual patient named in such order of such physician or dentist (or other specially qualified person so designated) and is to be made in a specific form for such patient, or

"(ii) is intended to meet the special needs of such physician or dentist (or other specially qualified person so designated) in the course of the professional prac-

tice of such physician or dentist (or other specially qualified person so designated), and

"(B) is not generally available to or generally used by other physicians or dentists (or other specially qualified persons so designated).

"Trade Secrets

"(c) Any information reported to or otherwise obtained by the Secretary or his representative under section 513, 514, 515, 516, 518, 519, or 704 or under subsection (f) or (g) of this section which is exempt from disclosure pursuant to subsection (a) of section 552 of title 5, United States Code, by reason of subsection (b)(4) of such section shall be considered confidential and shall not be disclosed and may not be used by the Secretary as the basis for the reclassification of a device under section 513 from class III to class II or as the basis for the establishment or amendment of a performance standard under section 514 for a device reclassified from class III to class II, except that such information may be disclosed to other officers or employees concerned with carrying out this Act or when relevant in any proceeding under this Act (other than section 513 or 514 thereof).

"Notices and Findings

"(d) Each notice of proposed rulemaking under section 513, 514, 515, 516, 518, or 519, or under this section, any other notice which is published in the Federal Register with respect to any other action taken under any such section and which states the reasons for such action, and each publication of findings required to be made in connection with rulemaking under any such section shall set forth—

"(1) the manner in which interested persons may examine data and other information on which the notice or findings is based, and

"(2) the period within which interested persons may present their comments on the notice or findings (including the need therefor) orally or in writing, which period shall be at least sixty days but may not exceed ninety days unless the time is extended stating good cause therefor.

"Restricted Devices

"(e)(1) The Secretary may by regulation require that a device be restricted to sale, distribution, or use—

"(A) only upon the written or oral authorization of a practitioner licensed by law to administer or use such device, or

"(B) upon such other conditions as the Secretary may prescribe in such regulation,

if, because of its potentiality for harmful effect or the collateral measures necessary to its use, the Secretary determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. No condition prescribed under subparagraph (B) may restrict the use of a device to persons with specific training or experience in its use or to persons for use in certain facilities unless the Secretary determines that such a restriction is required for the safe and effective use of the device. No such condition may exclude a person from using a device solely because the person does not have the training or experience to make him eligible for certification by a certifying board recognized by the American Board of Medical Specialties or has not been certified by such a Board. A device subject to a regulation under this subsection is a restricted device.

"(2) The label of a restricted device shall bear such appropriate statements of the restrictions required by a regulation under paragraph (1) as the Secretary may in such regulation prescribe.

"Good Manufacturing Practice Requirements

"(f)(1)(A) The Secretary may, in accordance with subparagraph (B), prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of a device conform to current good manufacturing practice, as prescribed in such regulations, to assure that the device will be safe and effective and otherwise in compliance with this Act.

"(B) Before the Secretary may promulgate any regulation under subparagraph (A) he shall—

"(i) afford the advisory committee established under paragraph (3) an opportunity to submit recommendations to him with respect to the regulation proposed to be promulgated, and

"(ii) afford opportunity for an oral hearing.

The Secretary shall provide the advisory committee a reasonable time to make its recommendation with respect to proposed regulations under subparagraph (A).

"(2)(A) Any person subject to any requirement prescribed by regulations under paragraph (1) may petition the Secretary for an exemption or variance from such requirement. Such a petition shall be submitted to the Secretary in such form and manner as he shall prescribe and shall—

"(i) in the case of a petition for an exemption from a requirement, set forth the basis for the petitioner's determination that compliance with the requirement is not required to assure that the device will be safe and effective and otherwise in compliance with this Act,

"(ii) in the case of a petition for a variance from a requirement, set forth the methods proposed to be used in, and the facilities and controls proposed to be

used for, the manufacture, packing, storage, and installation of the device in lieu of the methods, facilities, and controls prescribed by the requirement, and

"(iii) contain such other information as the Secretary shall prescribe.

"(B) The Secretary may refer to the advisory committee established under paragraph (3) any petition submitted under subparagraph (A). The advisory committee shall report its recommendations to the Secretary with respect to a petition referred to it within sixty days of the date of the petition referral. Within sixty days after—

"(i) the date the petition was submitted to the Secretary under subparagraph (A), or

"(ii) if the petition was referred to an advisory committee, the expiration of the sixty-day period beginning on the date the petition was referred to the advisory committee,

whichever occurs later, the Secretary shall by order either deny the petition or approve it.

"(C) The Secretary may approve—

"(i) a petition for an exemption for a device from a requirement if he determines that compliance with such requirement is not required to assure that the device will be safe and effective and otherwise in compliance with this Act, and

"(ii) a petition for a variance for a device from a requirement if he determines that the methods to be used in, and the facilities and controls to be used for, the manufacture, packing, storage, and installation of the device in lieu of the methods, controls, and facilities prescribed by the requirement are sufficeint to assure that the device will be safe and effective and otherwise in compliance with this Act.

An order of the Secretary approving a petition for a variance shall prescribe such conditions respecting the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of the device to be granted the variance under the petition as may be necessary to assure that the device will be safe and effective and otherwise in compliance with this Act.

"(D) After the issuance of an order under subparagraph (B) respecting a petition, the petitioner shall have an opportunity for an informal hearing on such order.

"(3) The Secretary shall establish an advisory committee for the purpose of advising and making recommendations to him with respect to regulations proposed to be promulgated under paragraph (1)(A) and the approval or disapproval of petitions submitted under paragraph (2). The advisory committee shall be composed of nine members as follows:

> "(A) Three of the members shall be appointed from persons who are officers or employees of any State or local government or of the Federal Government.
>
> "(B) Two of the members shall be appointed from persons who are representative of interests of the device manufacturing industry; two of the members shall be appointed from persons who are representative of the interests of physicians and other health professionals; and two of the members shall be representative of the interests of the general public.

Members of the advisory committee who are not officers or employees of the United States, while attending conferences or meetings of the committee or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent of the rate in effect for grade GS-18 of the General Schedule, for each day (including traveltime) they are so engaged; and while so serving away

from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 of the United States Code for persons in the Government service employed intermittently. The Secretary shall designate one of the members of the advisory committee to serve as its chairman. The Secretary shall furnish the advisory committee with clerical and other assistance. Section 14 of the Federal Advisory Committee Act shall not apply with respect to the duration of the advisory committee established under this paragraph.

"Exemption for Devices for Investigational Use

"(g)(1) It is the purpose of this subsection to encourage, to the extent consistent with the protection of the public health and safety and with ethical standards, the discovery and development of useful devices intended for human use and to that end to maintain optimum freedom for scientific investigators in their pursuit of that purpose.

"(2)(A) The Secretary shall, within the one hundred and twenty-day period beginning on the date of the enactment of this section, by regulation prescribe procedures and conditions under which devices intended for human use may upon application be granted an exemption from the requirements of section 502, 510, 514, 515, 516, 519, or 706 or subsection (e) or (f) of this section or from any combination of such requirements to permit the investigational use of such devices by experts qualified by scientific training and experienec to investigate the safety and effectiveness of such devices.

"(B) The conditions prescribed pursuant to subparagraph (A) shall include the following:

"(i) A requirement that an application be submitted to the Secretary before an exemption may be

granted [illegible] the application be submitted in such form and [illegible]er as the Secretary shall specify.

"(ii) A requirement that the person applying for an exemption for a device assure the establishment and maintenance of such records, and the making of such reports to the Secretary of data obtained as a result of the investigational use of the device during the exemption, as the Secretary determines will enable him to assure compliance with such conditions, review the progress of the investigation, and evaluate the safety and effectiveness of the device.

"(iii) Such other requirements as the Secretary may determine to be necessary for the protection of the public health and safety.

"(C) Procedures and conditions prescribed pursuant to subparagraph (A) for an exemption may appropriately vary depending on (i) the scope and duration of clinical testing to be conducted under such exemption, (ii) the number of human subjects that are to be involved in such testing, (iii) the need to permit changes to be made in the device subject to the exemption during testing conducted in accordance with a clinical testing plan required under paragraph (3)(A), and (iv) whether the clinical testing of such device is for the purpose of developing data to obtain approval for the commercial distribution of such device.

"(3) Procedures and conditions prescribed pursuant to paragraph (2)(A) shall require, as a condition to the exemption of any device to be the subject of testing involving human subjects, that the person applying for the exemption—

"(A) submit a plan for any proposed clinical testing of the device and a report of prior investigations of the device (including, where appropriate, tests on animals) adequate to justify the proposed clinical testing—

"(i) to the local institutional review committee which has been established in accordance with regulations of the Secretary to supervise clinical testing of devices in the facilities where the proposed clinical testing is to be conducted, or

"(ii) to the Secretary, if—

"(I) no such committee exists, or

"(II) the Secretary finds that the process of review by such committee is inadequate (whether or not the plan for such testing has been approved by such committee),

for review for adequacy to justify the commencement of such testing; and, unless the plan and report are submitted to the Secretary, submit to the Secretary a summary of the plan and a report of prior investigations of the device (including, where appropriate, tests on animals);

"(B) promptly notify the Secretary (under such circumstances and in such manner as the Secretary prescribes) of approval by a local institutional review committee of any clinical testing plan submitted to it in accordance with subparagraph (A);

"(C) in the case of a device to be distributed to investigators for testing, obtain signed agreements from each of such investigators that any testing of the device involving human subjects will be under such investigator's supervision and in accordance with subparagraph (D) and submit such agreements to the Secretary; and

"(D) assure that informed consent will be obtained from each human subject (or his representative) of proposed clinical testing involving such device, except where subject to such conditions as the Secretary may

prescribe, the investigator conducting or supervising the proposed clinical testing of the device determines in writing that there exists a life threatening situation involving the human subject of such testing which necessitates the use of such device and it is not feasible to obtain informed consent from the subject and there is not sufficient time to obtain such consent from his representative.

The determination required by subparagraph (I) shall be concurred in by a licensed physician who is not involved in the testing of the human subject with respect to which such determination is made unless immediate use of the device is required to save the life of the human subject of such testing and there is not sufficient time to obtain such concurrence.

"(4)(A) An application, submitted in accordance with the procedures prescribed by regulations under paragraph (2), for an exemption for a device (other than an exemption from section 516) shall be deemed approved on the thirtieth day after the submission of the application to the Secretary unless on or before such day the Secretary by order disapproves the application and notifies the applicant of the disapproval of the application.

"(B) The Secretary may disapprove an application only if he finds that the investigation with respect to which the application is submitted does not conform to procedures and conditions prescribed under regulations under paragraph (2). Such a notification shall contain the order of disapproval and a complete statement of the reasons for the Secretary's disapproval of the application and afford the applicant opportunity for an informal hearing on the disapproved order.

"(5) The Secretary may by order withdraw an exemption granted under this subsection for a device if the Secretary determines that the conditions applicable to the

device under this subsection for such exemption are not met. Such an order may be issued only after opportunity for an informal hearing, except that such an order may be issued before the provision of an opportunity for an informal hearing if the Secretary determines that the continuation of testing under the exemption with respect to which the order is to be issued will result in an unreasonable risk to the public health.

"Release of Safety and Effectiveness Information

"(h)(1) The Secretary shall promulgate regulatons under which a detailed summary of information respecting the safety and effectiveness of a device which information was submitted to the Secretary and which was the basis for—

"(A) an order under section 515(d)(1(A) approving an application for premarket approval for the device or denying approval of such an application or an order under section 515(e) withdrawing approval of such an application for the device,

"(B) an order under section 515(f)(6)(A) revoking an approved protocol for the device, an order under section 515(f)(6)(B) declaring a protocol for the device completed or not completed, or an order under section 515(f)(7) revoking the approval of the device, or

"(C) an order approving an application under subsection (g) for an exemption for the device from section 516 or an order disapproving, or withdrawing approval of, an application for an exemption under such subsection for the device,

shall be made available to the public upon issuance of the order. Summaries of information made available pursuant to this paragraph respecting a device shall include

information respecting any adverse effects on health of the device.

"(2) The Secretary shall promulgate regulations under which each advisory committee established under section 515(g)(2)(B) shall make available to the public a detailed summary of information respecting the safety and effectiveness of a device which information was submitted to the advisory committee and which was the basis for its recommendation to the Secretary made pursuant to section 515(g)(2)(A). A summary of information upon which such a recommendation is based shall be made available pursuant to this paragraph only after the issuance of the order with respect to which the recommendation was made and each summary shall include information respecting any adverse effect on health of the device subject to such order.

"(3) Ony information respecting a device which is made available pursuant to paragraph (1) or (2) of this subsection (A) may not be used to establish the safety or effectiveness of another device for purposes of this Act by any person other than the person who submitted the information so made available, and (B) shall be made available subject to subsection (c) of this section.

"Proceedings of Advisory Panels and Committees

"(i) Each panel under section 513 and each advisory committee established under section 514(g)(5)(B) or 515 (g) or under subsection (f) of this section shall make and maintain a transcript of any proceeding of the panel or committee. Each such panel and committee shall delete from any transcript made pursuant to this subsection information which under subsection (c) of this section is to be considered confidential.

"Traceability Requirements

"(j) No regulation under this Act may impose on a type or class of device requirements for the traceability of such type or class of device unless such requirements are necessary to assure the protection of the public health.

"Research and Development

"(k) The Secretary may enter into contracts for research, testing, and demonstrations respecting devices and may obtain devices for research, testing, and demonstration purposes without regard to sections 3648 and 3709 of the Revised Statutes (31 U.S.C. 529, 41 U.S.C. 5).

"Transitional Provisions for Devices Considered as New Drugs or Antibiotic Drugs

"(l)(1) Any device intended for human use—

"(A) for which on the date of enactment of the Medical Device Amendments of 1976 (hereinafter in this subsection referred to as the 'enactment date') an approval of an application submitted under section 505(b) was in effect;

"(B) for which such an application was filed on or before the enactment date and with respect to which application no order of approval or refusing to approve had been issued on such date under subsection (c) or (d) of such section;

"(C) for which on the enactment date an exemption under subsection (i) of such section was in effect;

"(D) which is within a type of device described in subparagraph (A), (B), or (C) and is substantially equivalent to another device within that type;

"(E) which the Secretary in a notice published in the Federal Register before the enactment date has declared to be a new drug subject to section 505; or

"(F) with respect to which on the enactment date an action is pending in a United States court under section 302, 303, or 304 for an alleged violation of a provision of section 301 which enforces a requirement of section 505 or for an alleged violation of section 505(a),

is classified in class III unless the Secretary in response to a petition submitted under paragraph (2) has classified such device in class I or II.

"(2) The manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition. Except as provided in paragraph (3)(D)(ii), within one hundred and eighty days after the filing of a petition under this paragraph and after affording the petitioner an opportunity for an informal hearing, the Secretary shall, after consultation with the appropriate panel under section 513, by order either deny the petition or order the classification, in accordance with the criteria prescribed by section 513(a)(1)(A) or 513(a)(1)(B), of the device in class I or class II.

"(3)(A) In the case of a device which is described in paragraph (1)(A) and which is in class III—

"(i) such device shall on the enactment date be considered a device with an approved application under section 515, and

"(ii) the requirements applicable to such device before the enactment date under section 505 shall continue to apply to such device until changed by the Secretary as authorized by this Act.

"(B) In the case of a device which is described in paragraph (1)(B) and which is in class III, an application for such device shall be considered as having been filed under section 515 on the enactment date. The period in which the Secretary shall act on such application in accordance with section 515(d)(1) shall be one hundred and eighty days from the enactment date (or such greater period as the Secretary and the applicant may agree upon after the Secretary has made the finding required by section 515(d)(1)(B)(i)) less the number of days in the period beginning on the date an application for such device was filed under section 505 and ending on the enactment date. After the expiration of such period such device is required, unless exempt under subsection (g), to have in effect an approved application under section 515.

"(C) A device which is described in paragraph (1)(C) and which is in class III shall be considered a new drug until the expiration of the ninety-day period beginning on the date of the promulgation of regulations under subsection (g) of this section. After the expiration of such period such device is required, unless exempt under subsection (g), to have in effect an approved application under section 515.

"(D)(i) Except as provided in clauses (ii) and (iii), a device which is described in subparagraph (D), (E), or (F) of paragraph (1) and which is in class III is required, unless exempt under subsection (g) of this section, to have on and after sixty days after the enactment date in effect an approved application under section 515.

"(ii) If—

"(I) a petition is filed under paragraph (2) for a device described in subparagraph (D), (E), or (F) of paragraph (1), or

"(II) an application for premarket approval is filed under section 515 for such a device,

within the sixty-day period beginning on the enactment date (or within such greater period as the Secretary, after making the finding required under section 515(d)(1)(B), and the petitioner or applicant may agree upon), the Secretary shall act on such petition or application in accordance with paragraph (2) or section 515 except that the period within which the Secretary must act on the petition or application shall be within the one hundred and twenty-day period beginning on the date the petition or application is filed. If such a petition or application is filed within such sixty-day (or greater) period, clause (i) of this subparagraph shall not apply to such device before the expiration of such one hundred and twenty-day period, or if such petition is denied or such application is denied approval, before the date of such denial, whichever occurs first.

"(iii) In the case of a device which is described in subparagraph (E) of paragraph (1), which the Secretary in a notice published in the Federal Register after March 31, 1976, declared to be a new drug subject to section 505, and which is in class III—

"(I) the device shall, after eighteen months after the enactment date, have in effect an approved application under section 515 unless exempt under subsection (g) of this section, and

"(II) the Secretary may, during the period beginning one hundred and eighty days after the enactment date and ending eighteen months after such date, restrict the use of the device to investigational use by

experts qualified by scientific training and experience to investigate the safety and effectiveness of such device, and to investigational use in accordance with the requirements applicable under regulations under subsection (g) of this section to investigational use of devices granted an exemption under such subsection.

If the requirements under subsection (g) of this section are made applicable to the investigational use of such a device, they shall be made applicable in such a manner that the device shall be made reasonably available to physicians meeting appropriate qualifications prescribed by the Secretary.

"(4) Any device intended for human use which on the enactment date was subject to the requirements of section 507 shall be subject to such requirements as follows:

"(A) In the case of such a device which is classified into class I, such requirements shall apply to such device until the effective date of the regulation classifying the device into such class.

"(B) In the case of such a device which is classified into class II, such requirements shall apply to such device until the effective date of a performance standard applicable to the device under section 514.

"(C) In the case of such a device which is classified into class III, such requirements shall apply to such device until the date on which the device is required to have in effect an approved application under section 515.

Chapter I—Food and Drug Administration

PART 860—MEDICAL DEVICE CLASSIFICATION PROCEDURES

Subpart A—General

Sec.

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860.136 Procedures for transitional products under section 520(l) of the act.

AUTHORITY: Secs. 513, 514, 515, 519, 520, and 701(a), 52 Stat. 1055, 90 Stat. 540-559, 564-574 (21 U.S.C. 360c, 360d, 360e, 360i, 360j, and 371(a)).

SOURCE: 43 FR 32993, July 28, 1978, unless otherwise noted.

Subpart A—General

§ 860.1 Scope.

(a) This part implements sections 513, 514(b), 515(b), and 520(l) of the act with respect to the classification and reclassification of devices intended for human use.

(b) This part prescribes the criteria and procedures to be used by classification panels in making their recommendations and by the Commissioner in making the Commissioner's determinations regarding the class of regulatory control (class I, class II, or class III) appropriate for particular devices. Supplementing the general Food and Drug Administration procedures governing advisory committees (part 14 of this chapter), this part also provides procedures for manufacturers, importers, and other interested persons to participate in proceedings to classify and reclassify devices. This part also describes the kind of data required for determination of the safety and effectiveness of a device, and the circumstances under which information submitted to classification panels or to the Commissioner in connection with classification and reclassification proceedings will be available to the public.

§ 860.3 Definitions.

For the purposes of this part:

(a) "Act" means the Federal Food, Drug, and Cosmetic Act.

(b) "Commissioner" means the Commissioner of Food and Drugs, Food and Drug Administration, United States Department of Health and Human Services, or the Commissioner's designee.

(c) "Class" means one of the three categories of regulatory control for medical devices, defined below:

(1) "Class 1" means the class of devices that are subject to only the general controls authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration), 516 (banned devices), 518 (notification and other remedies), 519 (records and reports), and 520 (general provisions) of the act. A device is in class I if (i) general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, or (ii) there is insufficient information from which to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish a performance standard to provide such assurance, but which is not life-supporting or life-sustaining or for a use which is of substanial importance in preventing impairment of human health, and which does not present a potential unreasonable risk of illness of injury.

(2) "Class II" means the class of devices that are or eventually will be subject to the requirements of a performance standard promulgated in accordance with section 514 of the act. A device is in class II if general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness and there is sufficient information to establish a performance standard to provide such assurance.

(3) "Class III" means the class of devices for which premarket approval is or will be required in accordance with section 515 of the act. A device is in class III if insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or to establish a performance standard to provide such assurance and if, in addition, the device is life-supporting of life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

(d) "Implant" means a device that is placed into a surgically or naturally formed cavity of the human body. A

device is regarded as an implant for the purpose of this part only if it is intended to remain implanted continuously for a period of 30 days or more, unless the Commissioner determines otherwise in order to protect human health.

(e) "Life-supporting or life-sustaining device" means a device that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life.

(f) "Classification questionnaire" means a specific series of questions prepared by the Commissioner for use as guidelines by classification panels preparing recommendations to the Commissioner regarding classification and by petitioners submitting petitions for reclassification. The questions relate to the safety and effectiveness characteristics of a device and the answers are designed to help the Commissioner determine the proper classification of the device.

(g) "Supplemental data sheet" means information compiled by a classification panel or submitted in a petition for reclassification, including:

(1) A summary of the reasons for the recommendation (or petition);

(2) A summary of the data upon which the recommendation (or petition) is based;

(3) An identification of the risks to health (if any) presented by the device;

(4) To the extent practicable in the case of a class II or class III device, a recommendation for the assignment of a priority for the application of the requirements of performance standards or premarket approval;

(5) In the case of a class I device, a recommendation whether the device should be exempted from any of the requirements of registration, record-keeping and reporting, or good manufacturing practice regulations;

(6) In the case of an implant or a life-supporting or life-sustaining device for which classification in class III is not recommended, a statement of the reasons for not recommending that the device be classified in class III;

(7) Identification of any needed restrictions on the use of the device, e.g., whether the device requires special labeling, should be banned, or should be used only upon authorization of a practitioner licensed by law to administer or use such device; and

(8) Any known existing standards applicable to the device, device components, or device materials.

(h) "Classification panel" means one of the several advisory committees established by the Commissioner under section 513 of the act and Part 14 of this chapter for the purpose of making recommendations to the Commissioner on the classification and reclassification of devices and for other purposes prescribed by the act or by the Commissioner.

(i) "Generic type of device" means a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness.

(j) "Petition" means a submission seeking reclassification of a device in accordance with § 860.123.

§ 860.5 Confidentiality and use of data and information submitted in connection with classification and reclassification.

(a) This section governs the availability for public disclosure and the use by the Commissioner of data and information submitted to classification panels or to the Commissioner in connection with the classification or reclassification of devices under this part.

(b) In general, data and information submitted to classification panels in connection with the classification of devices under § 860.84 will be available immediately for public disclosure upon request. However, except as provided by the special rules in paragraph (c) of this section, this provision does not apply to data and information exempt from public disclosure in accordance with Part 20 of this chapter: Such data and information will be available only in accordance with Part 20.

(c)(1) Safety and effectiveness data submitted to classification panels or to the Commissioner in connection with the classification of a device under § 860.84, which have not been disclosed previously to the public, as described in § 20.81 of this chapter, shall be regarded as confidential if the device is classified in to class III. Because the classification of a device under § 860.84 may be ascertained only upon publication of a final regulation, all safety and effectiveness data that have not been disclosed previously are not available for public disclosure unless and until the device is classified into class I or II, in which case the procedure in paragraph (c)(2) of this section applies.

(2) Thirty days after publication of a final regulation under § 860.84 classifying a device into class I or class II, safety and effectiveness data submitted for that device that had been regarded as confidential under paragraph (c)(1) of this section will be available for public disclosure and placed on public display in the office of the Dockets Management Branch, Food and Drug Administration unless, within that 30-day period, the person who submitted the data demonstrates that the data still fall within the exemption for trade secrets and confidential commercial information described in § 20.61 of this chapter. Safety and effectiveness data submitted for a device that is classified into class III by regulation in accordance with § 860.84 will remain confidential and unavailable for public disclosure so long as such data have not been disclosed to the public as described in § 20.81 of this chapter.

(3) Because device classification affects generic types of devices, in making determinations under § 860.84 concerning the initial classification of a device, the classification panels and the Commissioner may consider safety and effectiveness data developed for another device in the same generic type, regardless of whether such data are regarded currently as confidential under paragraph (c)(1) of this section.

(d)(1) The fact of its existence and the contents of a petition for reclassification filed in accordance with § 860.130 or § 860.132 are available for public disclosure at the time the petition is received by the Food and Drug Administration.

(2) The fact of the existence of a petition for reclassification filed in accordance with § 860.134 or § 860.136 is available for public disclosure at the time the petition is received by the Food and Drug Administration. The contents of such a petition are not available for public disclosure for the period of time following its receipt (not longer than 30 days) during which the petition is reviewed for any deficiencies preventing the Commissioner from making a decision on it. Once it is determined that the petition contains no deficiencies preventing the Commissioner from making a decision on it, the petition will be filed with the Dockets Management Branch and its entire contents will be available for public disclosure and subject to consideration by classification panels and by the Commissioner in making a decision on the petition. If, during this 30-day period of time, the petition is found to contain deficiencies that prevent the Commissioner from making a decision on it, the petitioner will be so notified and afforded an opportunity to correct the deficiencies.

Thirty days after notice to the petitioner of deficiencies in the petition, the contents of the petition will be available for public disclosure unless, within that 30 days, the petitioner submits supplemental material intended to

correct the deficiencies in the petition. The Commissioner, in the Commissioner's discretion, may allow withdrawal of a deficient petition during the 30-day period provided for correcting deficiencies. Any supplemental material submitted by the petitioner, together with the material in the original petition, is considered as a new petition. The new petition is reviewed for deficiencies in the same manner as the original petition, and the same procedures for notification and correction of deficiencies are followed. Once the petitioner has corrected the deficiencies, the entire contents of the petition will be available for public disclosure and subject to consideration by classification panels and by the Commissioner in making a decision on the petition. Deficient petitions which have not been corrected within 180 days after notification of deficiency will be returned to the petitioner and will not be considered further unless resubmitted.

(e) The Commissioner may not disclose, or use as the basis for reclassification of a device from class III to class II, any information reported to or otherwise obtained by the Commissioner under section 513, 514, 515, 516, 518, 519, 520(f), 520(g), or 704 of the act that falls within the exemption described in § 20.61 of this chapter for trade secrets and confidential commercial information. The exemption described in § 20.61 does not apply to data or information contained in a petition for reclassification submitted in accordance with § 860.130 or § 860.132, or in a petition submitted in accordance with § 860.134 or § 860.136 that has been determined to contain no deficiencies that prevent the Commissioner from making a decision on it. Accordingly, all data and information contained in such petitions may be disclosed by the Commissioner and used as the basis for reclassification of a device from class III to class II.

(f) For purposes of this section, safety and effectiveness data include data and results derived from all studies and tests of a device on animals and humans and from all

studies and tests of the device itself intended to establish or determine its safety and effectiveness.

§ 860.7 Determination of safety and effectiveness.

(a) The classification panels, in reviewing evidence concerning the safety and effectiveness of a device and in preparing advice to the Commissioner, and the Commissioner, in making determinations concerning the safety and effectiveness of a device, will apply the rules in this section.

(b) In determining the safety and effectiveness of a device for purposes of classification, establishment of performance standards for class II devices, and premarket approval of class III devices, the Commissioner and the classification panels will consider the following, among other relevant factors:

(1) The persons for whose use the device is represented or intended;

(2) The conditions of use for the device, including conditions of use prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use;

(3) The probable benefit to health from the use of the device weighed against any probable injury or illness from such use; and

(4) The reliability of the device.

(c)(1) Although the manufacturer may submit any form of evidence to the Food and Drug Administration in an attempt to substantiate the safety and effectiveness of a device, the agency relies upon only valid scientific evidence to determine whether there is reasonable assurance that the device is safe and effective. After considering the nature of the device and the rules in this section, the Commissioner will determine whether the evidence submitted or otherwise available to the Commissioner is valid scientific evidence

for the purpose of determining the safety or effectiveness of a particular device and whether the available evidence, when taken as a whole, is adequate to support a determination that there is reasonable assurance that the device is safe and effective for its conditions of use.

(2) Valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness. Such information may be considered, however, in identifying a device the safety and effectiveness of which is questionable.

(d)(1) There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use.

(2) Among the types of evidence that may be required, when appropriate, to determine that there is reasonable assurance that a device is safe are investigations using

laboratory animals, investigations involving human subjects, and nonclinical investigations including in vitro studies.

(e)(1) There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.

(2) The valid scientific evidence used to determine the effectiveness of a device shall consist principally of well-controlled investigations, as defined in paragraph (f) of this section, unless the Commissioner authorizes reliance upon other valid scientific evidence which the Commissioner has determined is sufficient evidence from which to determine the effectiveness of a device, even in the absence of well-controlled investigations. The Commissioner may make such a determination where the requirement of well-controlled investigations in paragraph (f) of this section is not reasonably applicable to the device.

(f) The following principles have been developed over a period of years and are recognized by the scientific community as the essentials of a well-controlled clinical investigation. They provide the basis for the Commissioner's determination whether there is reasonable assurance that a device is effective based upon well-controlled investigations and are also useful in assessing the weight to be given to other valid scientific evidence permitted under this section.

(1) The plan or protocol for the study and the report of the results of a well-controlled investigation shall include the following:

(i) A clear statement of the objectives of the study;

(ii) A method of selection of the subjects that:

(*a*) Provides adequate assurance that the subjects are suitable for the purposes of the study, provides diagnostic criteria of the condition to be treated or diagnosed, provides confirmatory laboratory tests where appropriate and, in the case of a device to prevent a disease or condition, provides evidence of susceptibility and exposure to the condition against which prophylaxis is desired;

(*b*) Assigns the subjects to test groups, if used, in such a way as to minimize any possible bias;

(*c*) Assures comparability between test groups and any control groups of pertinent variables such as sex, severity or duration of the disease, and use of therapy other than the test device;

(iii) An explanation of the methods of observation and recording of results utilized, including the variables measured, quantitation, assessment of any subject's response, and steps taken to minimize any possible bias of subjects and observers;

(iv) A comparison of the results of treatment or diagnosis with a control in such a fashion as to permit quantitative evaluation. The precise nature of the control must be specified and an explanation provided of the methods employed to minimize any possible bias of the observers and analysts of the data. Level and methods of "blinding," if appropriate and used, are to be documented. Generally, four types of comparisons are recognized:

(*a*) *No treatments.* Where objective measurements of effectiveness are available and placebo effect is negligible, comparison of the objective results in comparable groups of treated and untreated patients;

(*b*) *Placebo control.* Where there may be a placebo effect with the use of a device, comparison of the results of use of the device with an ineffective device used under conditions designed to resemble the conditions of use under investigation as far as possible;

(*c*) *Active treatment control.* Where an effective regimen of therapy may be used for comparison, e.g., the condition being treated is such that the use of a placebo or the withholding of treatment would be inappropriate or contrary to the interest of the patient;

(*d*) *Historical control.* In certain circumstances, such as those involving diseases with high and predictable mortality or signs and symptoms of predictable duration or severity, or in the case of prophylaxis where morbidity is predictable, the results of use of the device may be compared quantitatively with prior experience historically derived from the adequately documented natural history of the disease or condition in comparable patients or populations who received no treatment or who followed an established effective regimen (therapeutic, diagnostic, prophylactic).

(v) A summary of the methods of analysis and an evaluation of the data derived from the study, including any appropriate statistical methods utilized.

(2) To insure the reliability of the results of an investigation, a well-controlled investigation shall involve the use of a test device that is standardized in its composition or design and performance.

(g)(1) It is the responsibility of each manufacturer and importer of a device to assure that adequate, valid scientific evidence exists, and to furnish such evidence to the Food and Drug Administration to provide reasonable assurance that the device is safe and effective for its intended uses and conditions of use. The failure of a manufacturer or importer of a device to present to the Food and Drug Administration adequate, valid scientific evidence showing that there is reasonable assurance of the safety and effectiveness of the device, if regulated by general controls alone, or by general controls and performance standards, may support a determination that the device be classified into class III.

(2) The Commissioner may require that a manufacturer, importer, or distributor make reports or provide other information bearing on the classification of a device and indicating whether there is reasonable assurance of the safety and effectiveness of the device or whether it is adulterated or misbranded under the act.

(3) A requirement for a report or other information under this paragraph will comply with section 519 of the act. Accordingly, the requirement will state the reason or purpose for such request; will describe the required report or information as clearly as possible; will not be imposed on a manufacturer, importer, or distributor of a classified device that has been exempted from such a requirement in accordance with § 860.95; will prescribe the time for compliance with the requirement; and will prescribe the form and manner in which the report or information is to be provided.

(4) Required information that has been submitted previously to the Bureau of Medical Devices need not be resubmitted, but may be incorporated by reference.

Subpart B—Classification

§ 860.84 Classification procedures for "old devices."

(a) This subpart sets forth the procedures for the original classification of a device that either was in commercial distribution before May 28, 1976, or is substantially equivalent to a device that was in commercial distribution before that date. Such a device will be classified by regulation into either class I (general controls), class II (performance standards), or class III (premarket approval), depending upon the level of regulatory control required to provide reasonable assurance of the safety and effectiveness of the device (§ 860.3(c)). This subpart does not apply to a device that is classified into class III by statute under section 513(f) of the act because the Food and Drug Administration has determined that the device is not "substantially

equivalent" to any device subject to this subpart or under section 520(l)(1) through (3) of the act because the device was regarded previously as a new drug. This subpart does apply to a device that was previously regarded as an antibiotic drug and that is subject to section 520(l)(4) of the act. In classifying a device under this section, the Food and Drug Administration will follow the procedures described in paragraphs (b) through (g) of this section.

(b) The Commissioner refers the device to the appropriate classification panel organized and operated in accordance with section 513(b) and (c) of the act and Part 14 of this chapter.

(c) In order to make recommendations to the Commissioner on the class of regulatory control (class I, class II, or class III) appropriate for the device, the panel reviews the device for safety and effectiveness. In so doing, the panel:

(1) Considers the factors set forth in § 860.7 relating to the determination of safety and effectiveness;

(2) Determines the safety and effectiveness of the device on the basis of the types of scientific evidence set forth in § 860.7;

(3) Answers the questions in the classification questionnaire applicable to the device being classified;

(4) Completes a supplemental data sheet for the device;

(5) Provides, to the maximum extent practicable, an opportunity for interested persons to submit data and views on the classification of the device in accordance with Part 14 of this chapter.

(d) Based upon its review of evidence of the safety and effectiveness of the device, and applying the definition of each class in § 860.3(c), the panel submits to the Commis-

sioner a recommendation regarding the classification of the device. The recommendation will include:

(1) A summary of the reasons for the recommendation;

(2) A summary of the data upon which the recommendation is based, accompanied by references to the sources containing such data;

(3) An identification of the risks to health (if any) presented by the device;

(4) In the case of a recommendation for classification into class I, a recommendation as to whether the device should be exempted from the requirements of one or more of the following sections of the act: section 510 (registration, product listing, and premarket notification) section 519 (records and reports) and section 520(f) (good manufacturing practice regulations) in accordance with § 860.95;

(5) In the case of a recommendation for classification into class II or class III, to the extent practicable, a recommendation for the assignment to the device of a priority for the application of a performance standard or a premarket approval requirement;

(6) In the case of a recommendation for classification of an implant or a life-supporting or life-sustaining device into class I or class II, a statement of why premarket approval is not necessary to provide reasonable assurance of the safety and effectiveness of the device, accompanied by references to supporting documentation and data satisfying the requirements of § 860.7, and an identification of the risks to health, if any, presented by the device.

(e) A panel recommendation is regarded as preliminary until the Commissioner has reviewed it, discussed it with the panel if appropriate, and published a proposed regulation classifying the device. Preliminary panel recommendations are filed in the Dockets Management Branch's office upon receipt and are available to the public upon request.

(f) The Commissioner publishes the panel's recommendation in the FEDERAL REGISTER, together with a proposed regulation classifying the device, and other devices of that generic type, and provides interested persons an opportunity to submit comments on the recommendation and proposed regulation.

(g) The Commissioner reviews the comments and issues a final regulation classifying the device and other devices of that generic type. The regulation will:

(1) If classifying the device into class I, prescribe which, if any, of the requirements of sections 510, 519, and 520(f) of the act will not apply to the device and state the reasons for making the requirements inapplicable, in accordance with § 860.95;

(2) If classifying the device into class II or class III, at the discretion of the Commissioner, establish priorities for the application to the device of a performance standard or a premarket approval requirement;

(3) If classifying an implant, or life-supporting or life-sustaining device, comply with § 860.93(b).

§ 860.93 Classification of implants, life-supporting or life-sustaining devices.

(a) The classification panel will recommend classification into class III of any implant or life-supporting or life-sustaining device unless the panel determines that such classification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. If the panel recommends classification or reclassification of such a device into a class other than class III, it shall set forth in its recommendation the reasons for so doing together with references to supporting documentation and data satisfying the requirements of § 860.7, and an identification of the risks to health, if any, presented by the device.

(b) The Commissioner will classify an implant or life-supporting or life-sustaining device into class III unless the Commissioner determines that such classification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. If the Commissioner proposes to classify or reclassify such a device into a class other than class III, the regulation or order effecting such classification or reclassification will be accompanied by a full statement of the reasons for so doing. A statement of the reasons for not classifying or retaining the device in class III may be in the form of concurrence with the reasons for the recommendation of the classification panel, together with supporting documentation and data satisfying the requirements of § 860.7 and an identification of the risks to health, if any, presented by the device.

§ 860.95 Exemptions from sections 510, 519, and 520(f) of the act.

(a) A panel recommendation to the Commissioner that a device be classified or reclassified into class I will include a recommendation as to whether the device should be exempted from some or all of the requirements of one or more of the following sections of the act: Section 510 (registration, product listing and premarket notification), section 519 (records and reports), and section 520(f) (good manufacturing practice regulations).

(b) A regulation or an order classifying or reclassifying a device into class I will specify which requirements, if any, of sections 510, 519, and 520(f) of the act the device is to be exempted from, together with the reasons for such exemption.

(c) The Commissioner will grant exemptions under this section only if the Commissioner determines that the requirements from which the device is exempted are not necessary to provide reasonable assurance of the safety and effectiveness of the device.

Subpart C—Reclassification

§ 860.120 General.

(a) Sections 513(e) and (f), 514(b), 515(b), and 520(l) of the act provide for reclassificaton of a device and prescribe the procedures to be followed to effect reclassification. The purposes of Subpart C are to:

(1) Set forth the requirements as to form and content of petitions for reclassification;

(2) Describe the circumstances in which each of the five statutory reclassification provisions applies; and

(3) Explain the procedure for reclassification prescribed in the five statutory reclassification provisions.

(b) The criteria for determining the proper class for a device are set forth in § 860.3(c). The reclassification of any device within a generic type of device causes the reclassification of all substantially equivalent devices within that generic type. Accordingly, a petition for the reclassification of a specific device will be considered a petition for reclassification of all substantially equivalent devices within the same generic type.

(c) Any interested person may submit a petition for reclassification under section 513(e), 514(b), or 515(b). A manufacturer or importer may submit a petition for reclassification under section 513(f) or 520(l).

§ 860.123 Reclassification petition: Content and form.

(a) Unless otherwise provided in writing by the Commissioner, any petition for reclassification of a device, regardless of the section of the act under which it is filed, shall include the following:

(1) A specification of the type of device for which reclassification is requested;

(2) A statement of the action requested by the petitioner, e.g., "It is requested that — device(s) be reclassified from class III to a class II";

(3) A completed supplemental data sheet applicable to the device for which reclassification is requested;

(4) A completed classification questionnaire applicable to the device for which reclassification is requested;

(5) A statement of the basis for disagreemnt with the present classification status of the device;

(6) A full statement of the reasons, together with supporting data satisfying the requirements of § 860.7, why the device should not be classified into its present classification and how the proposed classification will provide reasonable assurance of the safety and effectiveness of the device;

(7) Representative data and information known by the petitioner that are unfavorable to the petitioner's position;

(8) If the petition is based upon new information under section 513(e), 514(b), or 515(b) of the act, a summary of the new information;

(9) Copies of source documents from which new information used to support the petition has been obtained (attached as appendices to the petition).

(b) Each petition submitted pursuant to this section shall be:

(1) Addressed to the Food and Drug Administration, Bureau of Medical Devices, Document Control Center (HFK-20), 8757 Georgia Avenue, Silver Spring, Md. 20910;

(2) Marked clearly with the section of the act under which the petition is being submitted, i.e., "513(e)," "513 (f)," "514(b)," "515(b)," or "520(l) Petition";

(3) Bound in a volume or volumes, where necessary; and

(4) Submitted in quintuplicate.

§ 860.125 Consultation with panels.

(a) When the Commissioner is required to refer a reclassification petition to a classification panel for its recommendation under § 860.134, or is required, or chooses, to consult with a panel concerning a reclassification petition, such as under § 860.130, § 806.132, or § 860.136, the Commissioner will distribute a copy of the petition, or its relevant portions, to each panel member and will consult with the panel in one of the following ways:

(1) Consultation by telephone with at least a majority of current voting panel members and, when possible, nonvoting panel members;

(2) Consultation by mail with at least a majority of current voting panel members and, when possible, nonvoting panel members; and

(3) Discussion at a panel meeting.

(b) The mething of consultation chosen by the Commissioner will depend upon the importance and complexity of the subject matter involved and the time available for action. When time and circumstances permit, the Commissioner will consult with a panel through discussion at a panel meeting.

(c) When a petition is submitted under § 860.134 for a post-enactment, not substantially equivalent device ("new device"), in consulting with the panel the Commissioner will obtain a recommendation that includes the information described in § 860.84(d). In consulting with a panel about a petition submitted under § 860.130, § 860.132, or § 860.136, the Commissioner may or may not obtain a formal recommendation.

§ 860.130 General procedures under section 513(e) of the act.

(a) Section 513(e) of the act applies to reclassification proceedings under the act based upon new information.

(b) A proceeding to reclassify a device under section 513(e) may be initiated:

(1) On the initiative of the Commissioner alone;

(2) On the initiative of the Commissioner in response to a request for change in classification based upon new information, under section 514(b) or 515(b) of the act (see § 860.132); or

(3) In response to the petition of an interested person, based upon new information, filed in accordance with § 860.123.

(c) The rulemaking procedures in § 10.40 of this chapter apply to proceedings to reclassify a device under section 513(e), except that the Commissioner may secure a recommendation with respect to a proposed reclassification from the classification panel to which the device was last referred. The panel will consider a proposed reclassification submitted to it by the Commissioner in accordance with the consultation procedures of § 860.125. Any recommendation submitted to the Commissioner by the panel will be published in the FEDERAL REGISTER when the Commissioner promulgates a regulation under this section.

(d) Within 180 days after the filing of a petition for reclassificaton under this section, the Commissioner, by order published in the FEDERAL REGISTER, will either deny the petition ro give notice of his intent to initiate a change in the classfication of the device.

(e) If a device is reclassified under this section, the regulation effecting the reclassification may revoke any performance standard or premarket approval requirement

that previously applied to the device but that is no longer applicable because of the change in classification.

(f) A regulation under this section changing the classification of a device from class III to class II may provide that such classification will not take effect until the effective date of a performance standard for the device established under section 514 of the act.

§ 860.132 Procedures when the Commissioner initiates a performance standard or premarket approval proceeding under section 514(b) or 515(b) of the act.

(a) Sections 514(b) and 515(b) of the act require the Commissioner to provide, by notice in the FEDERAL REGISTER, an opportunity for interested parties to request a change in the classification of a device based upon new information relevant to its classification when the Commissioner initiates a proceeding either to develop a performance standard for the device if in class II, or to promulgate a regulation requiring premarket approval for the device if in class III. In either case, if the Commissioner agrees that the new information warrants a change in classification, the Commissioner will publish in the FEDERAL REGISTER notice of the Commissioner's intent to initiate a proceeding under section 513(e) of the act and § 860.130 to effect such a change.

(b) The procedures for effecting a change in classification under sections 514(b) and 515(b) of the act are as follows:

(1) Within 15 days after publication of the Commissioner's notice referred to in paragraph (a) of this section, an interested person files a petition for reclassification in accordance with § 860.123.

(2) The Commissioner consults with the appropriate classification panel with regard to the petition in accordance with § 860.125.

(3) Within 60 days after publication of the notice referred to in paragraph (a) of this section, the Commissioner, by order published in the FEDERAL REGISTER, either denies the petition or gives notice of his intent to initiate a change in classification in accordance with § 860.130.

§ 860.134 Procedures for "new devices" under section 513(f) of the act.

(a) Section 513(f)(2) of the act applies to reclassification proceedings initiated by a manufacturer or importer for reclassification of a device currently in class III by operation of section 513(f)(1) of the act. This category includes any device that is to be first introduced or delivered for introduction into interstate commerce for commercial distribution after May 28, 1976, unless:

(1) It is substantially equivalent to another device that was in commercial distribution before that date and had not been regulated before that date as a new drug; or

(2) It is substantially equivalent to another device that was not in commercial distribution before such date but which has been classified into class I or class II; or

(3) The Commissioner has classified the device into class I or class II in response to a petition for reclassification under this section.

The Commissioner determines whether a device is "substantially equivalent" for purposes of the application of this section. If a manufacturer or importer believes that a device is not "substantially equivalent" but that it should not be in class III under the criteria in § 860.3(c), the manufacturer or importer may petition for reclassification under this section. A manufacturer or importer who believes that a device is "substantially equivalent" and wishes to proceed to market the device shall submit a premarket notification in accordance with Part 807 of this

chapter. After considering a premarket notification, the Commissioner will determine whether the device is "substantially equivalent" and will notify the manufacturer or importer of such determination in accordance with Part 807 of this chapter.

(b) The procedures for effecting reclassification under section 513(f) of the act are as follows:

(1) The manufacturer or importer of the device petitions for reclassification of the device in accordance with § 860.123.

(2) Within 30 days after the petition is filed, the Commissioner notifies the petitioner of any deficiencies in the petition that prevent the Commissioner from making a decision on it and allows the petitioner to supplement a deficient petition. Within 30 days after any supplemental material is received, the Commissioner notifies the petitioner whether the petition, as supplemented, is adequate for review.

(3) After determining that the petition contains no deficiencies precluding a decision on it, the Commissioner refers the petition to the appropriate classification panel for its review and recommendation whether to approve or deny the petition.

(4) Within 90 days after the date the petition is referred to the panel, following the review procedures set forth in § 860.84(c) for the original classification of an "old" device, the panel submits to the Commissioner its recommendation containing the information set forth in § 860.84(d). A panel recommendation is regarded as preliminary until the Commissioner has reviewed it, discussed it with the panel, if appropriate, and developed a proposed reclassification order. Preliminary panel recommendations are filed in the Dockets Management Branch upon receipt and are available to the public upon request.

(5) The panel recommendation is published in the FEDERAL REGISTER as soon as practicable and interested persons are provided an opportunity to comment on the recommendation.

(6) Within 90 days after the panel's recommendation is received (and no more than 210 days after the date the petition was filed), the Commissioner denies or approves the petition by order in the form of a letter to the petitioner. If the Commissioner approves the petition, the order will classify the device into class I or class II in accordance with the criteria set forth in § 860.3(c) and subject to the applicable requirements of § 860.93, relating to the classification of implants, life-supporting or life-sustaining devices, and § 860.95, relating to exemptions from certain requirements of the act.

(7) Within a reasonable time after issuance of an order under this section, the Commissioner announces the order by notice published in the FEDERAL REGISTER.

§ 860.136 Procedures for transitional products under section 520(l) of the act.

(a) Section 520(l)(2) of the act applies to reclassification proceedings initiated by a manufacturer or importer for reclassification of a device currently in class III by operation of section 520(l)(1) of the act. This section applies only to devices that the Food and Drug Administration regarded as "new drugs" before May 28, 1976.

(b) The procedures for effecting reclassification under section 520(l) are as follows:

(1) The manufacturer or importer of the device files a petition for reclassification of the device in accordance with § 860.123.

(2) Within 30 days after the petition is filed, the Commissioner notifies the petitioner of any deficiences in the

petition that prevent the Commissioner from making a decision on it, allowing the petitioner to supplement a deficient petition. Within 30 days after any supplemental material is received, the Commissioner notifies the petitioner whether the petition, as supplemented, is adequate for review.

(3) The Commissioner provides the petitioner an opportunity for a regulatory hearing conducted in accordance with Part 16 of this chapter.

(4) The Commissioner consults with the appropriate classification panel with regard to the petition in accordance with § 860.125.

(5) Within 180 days after the petition is filed (where the Commissioner has determined it to be adequate for review), the Commissioner, by order in the form of a letter to the petitioner, either denies the petition or classifies the device into class I or class II in accordance with the criteria set forth in § 860.3(c).

(6) Within a reasonable time after issuance of an order under this section, the Commissioner announces the order by notice published in the FEDERAL REGISTER.